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CONTENTS IN BRIEF

Editorial

Flipped Learning in Continuing Medical Education

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Abstract

In order to increase the effectiveness of Continuing Medical Education, the department of education in Tungs' Hospital applies the flipped learning approach to different fields of continuing medical education and trainings. One of the main goals of the flipped learning approach is to seek learning in both breadth and depth. Participants can utilize what they have learned in their workshop to increase the quality of medical care for their patients. One of the differences between flipped learning and traditional teaching is that the learners study the content at their own convenience. Those learning materials are delivered via videos or other e-learning platforms. In the flipped learning class or workshop, the interactive learning activities and discussions are the main foci in place of the traditional lecture model. The goal of the flipped learning model is to encourage learners to take initiative of their learning through updating their medical knowledge and patient care skills, thus making Continuing Medical Education truly meaningful.

Key words: Flipped learning, Interactive learning, Continuing medical education

Continuing medical education (CME) is an opportunity to help those in the medical field maintain competence and learn the updated knowledge of their field. It can be a challenge for current continuing medical education to provide a high quality CME and make it available to medical professionals who have different work schedules and locations. With the increase of digital learning at many institutes in most developed countries, the literature on using flipped learning in higher professional education has been growing quickly. The basic model of flipped learning is that apprentices learn new content outside of classroom or workshop, and instructors spend more class or workshop time to engage learners in deeper discussions, hands-on application, and case analysis. One strong advantage of flipped learning is that learners are able to receive material and study it in their own location and pace. This can also promote convenience as it reduces the needed time to be physically present in classes or workshops. It makes continuing medical education more accessible to busy professionals[1-3]. By taking the lecture portion of learning at home, learners can gather questions and prepare themselves for the day of the class or workshop, where they can discuss important concepts, confusion, or difficulties of the topic with their instructors. Specifically, learners can receive direct input on those areas of the material that are most difficult or ambiguous during the in-class or workshop discussion to make their learning more effective[4]. The process of flipped learning includes preparation, pre-class learning, in-class learning, and assessment (Figure 1). The following paragraphs will discuss more details about each process.

Preparation of Flipped Learning

The readiness of both instructors and learners of flipped learning is an essential factor of success for this learning model. In order to implement flipped learning model successfully, instructors need to be capable of performing certain level of technical skills, knowledge, and teaching technique of flipped learning. Offering a session of related training will

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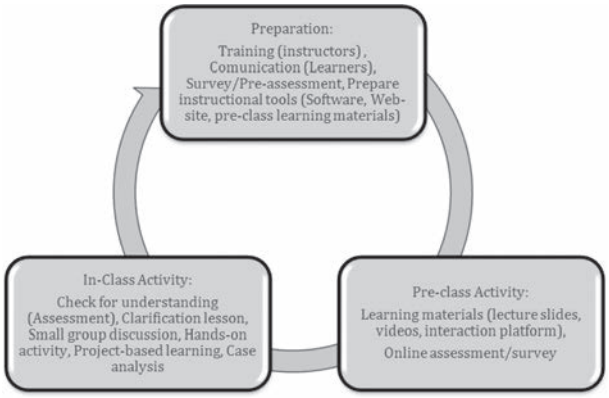

Fig. 1 Process of Flipped Learning

be the first step of implementing this learning approach[5]. In addition, many learners, especially in Asian countries, may be resistant to active learning activity in classes or workshops, because we are so used to lecture-based learning from elementary schools up to even graduate or professional schools. Therefore, a clear explanation of the reason for this structure of continuing education program and the benefits of such model is important to learners prior to the start of the program.

One of the most important instructional decisions that instructors will encounter is how to choose learning materials for pre-class assignments and design in-class interactive activities. A pre-assessment or survey during the registration of the program is critical for gathering information about program participants in their abilities and background knowledge. The information includes learning habits, working experience, comfort level of using technology, and certain pre-requisite content knowledge of the topics in the program. This data will be tremendously helpful for determining appropriate pre-class materials and planning in class or workshop learning experience for learners.

Pre-class Learning

One essential components of flipped learning is to offer an opportunity for learners to learn lesson related material at their own pace and on their own time before going to class or workshop. For pre-class learning material, it is not necessary to just use technology. A combination of traditional article reading with online lecture slide or video watching also can be an effective way to provide pre-class learning material. In order to maximum the efficiency of pre-class learning, instructors need to explicitly give a focused goal and the types of achievement needed to be performed before they meet in the class/workshop. Therefore, instructors need to think about what they expect learners to be able to do by the end of the pre-class session, and if the materials fully support the learning objectives and prepare learners with the basic concept and necessary skills. Using technology is a major tool for designing pre-class materials. As the result, there is additional work involved in creating online materials. Different software and platforms will serve different function for pre-class material or activity. Software such as Microsoft Power Point, iMovie, and Podcast are very popular tools for creating lecture slides and videos. In addition to self-produce teaching material, we can also get some useful resource from YouTube, Podcast, or iTunes U. Once we have the materials, we can use links, Dropbox, or Google Classroom to share or distribute pre-class materials. In the pre-class session, online discussion is also one way to engage each individual's learning. Blackboard and Padlet are widely used platforms by many academic institutions for student online interaction purposes. Some higher education institutions also provide face-to-face session online for flipped learning. Webinar or Skype are used very often in conference calls to do online training and communication.

In-Class or Workshop Activities

In the Flipped Learning model, the traditional content learning has been turned into at-home activities. People might be wondering what instructors and learners are or should be doing during class or workshop. In a continuing medical education program, the in-workshop activities can be a check for understanding (assessment), a clarification moment, small group discussion of pre-class learning material, project-base learning, hands-on activity, case analysis…etc[6]. (Table 1)

One of the issues of Flipped Learning is that the learning model requires learners to be self motivated for their own learning. It will be ineffective if the learners fail to engage with the assigned pre-class activity. It may be a challenge for instructors to make pre-class activity accountable while, nevertheless,

Table 1. Examples for In-class or Workshop Activities of Flipped Learning

Activity	Examples
Check for Understanding	Individual: Quiz for assessing students' understanding of the pre-class assignment.
	Pair/Group: Discuss and answer the questions on the discussion sheet.
Clarification Moment	Whole group instruction: Provide short mini lesson clarify the misconception or difficult content of pre-class assignment.
	Whole group discussion: Provide time for learners to ask questions that they have in the assigned material; instructor or other learners will provide input for the questions asked
Hands-on Activities	Provide hands-on practice for the medical skills that they learned from pre-class learning materials:
	Example: If the topic of the learning is "How to identify types of heart diseases from EKG test," the hands-on activity can be providing a set of different EKG reports among with some supported medical information to ask learners to identify the types of heart disease
Project-based Learning	Pair/small group activity: Provide a project that learners can complete and present during the workshop time. In the activity, learners can see each other's project and communicate with their colleagues to make improvement of their project
	Example: If the learning topic is "Nutrition for diabetes patients," the project can be designing a weekly meal plan for different diabetes patients combining other health issues.
Case analysis	Pair/small group activity: Provide some real cases for learners to apply their learning result from pre-class learning material to analyze clinical cases.
	Example: If the learning topic is Headache, the activity can ask learners to discuss how the presentation of headache can offer clues to the diagnosis; and how to prescribe appropriate medical therapy for preventive, acute, and rescue treatment.

engaging learners who did not complete the pre-class assignment. An important principle of in-class activity of flipped learning is to not revert back to lecturing. Otherwise, learners will not come prepared for future classes. Instructor can provide a brief lesson to clarify confusion or explain difficult concepts of the assigned materials but avoid re-teaching the basics. Peer instruction is another strategy that can be used. Learners will be divided in to pairs or small groups for this activity. During the peer instruction activity, learners not only have opportunity to catch up the concepts that they failed to learn in pre-class material, but also allow these individuals to realize the effort that their colleagues made for the learning in order to encourage them complete their assignments before coming to the workshop next time.

Evaluation

Similar to any traditional education model, frequent formative assessment is a key chain that connects each segment of the learning process. Using frequent formative assessment to determine each learner's needs to design and provide appropriate learning material and activity is a crucial instrument to make the lesson more successful. As I mentioned in the previous paragraph, a pre-assessment or survey should be done to collect the participants' information and background knowledge about the topics for the workshop. Instructors will use the information to create pre-class material and activity. In the pre-class learning session, some simple formative assessments also need to be administered after learners finish their study. Learners can post their response on Blackboard or Padlet in an anonymous way. The questions on this session can be very open-ended, such as "What is the most important thing you learned from pre-class material?" and "What is most confusing to you in the material?" From the response that learners post, instructors can use the data to analyze what misconceptions and difficulties that learners have in order to design their in-class clarification lesson and activities.

Checking for understanding is almost a universal first class activity cross-different subjects and age levels in flipped learning classes/workshop. The

depth of knowledge assessed here is more than the assessment in pre-class learning session. Since it is an in-class assessment, instructors can clearly observe how much each learner understands. They can also gauge if the knowledge and skills that the individuals currently possess is sufficient to support them for the in-class activities. After a quick overview, the instructor will decide how long and what the clarification lesson is to be able to meet the learners' needs. The assessment method can be a very traditional paper and pencil test. Since the purpose of the test is to check for understanding, the questions should focus on assessing learners' comprehension instead of their memorization of the material. One example question can be asking learners to write a layman's "translation" of something they have just learned for a patient or patient family in order to evaluate learners' ability to comprehend and transfer concepts.

Conclusion

Flipped learning is a teaching approach in which the whole group instruction moves from traditional classroom setting to individual learning environment with a self pacing speed. In this approach, the main lecture of the learning topic that students gain is from outside of workshop, mostly through online video or reading. The flexibility of self-pace and learning space reduces the time for medical professionals to be physically present in a medical education program. Thus, this allows for more efficiency and convenience for individuals to participate in workshops. In a flipped learning model, formative assessments play a key role to collect evidence of learning and offer significant data for each stage of lesson design. Prior to the implementation of a flipped learning model, training should be provided for instructors to enhance their technology skills and learn the concept and teaching model of the flipped learning approach [7]. With greater application of fundamental concepts, meaningful interaction between learners and instructor, and collaboration increased among learners in the workshop activities, flipped learning is another channel for current continuing medical education.

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醫學繼續教育之翻轉教學法

遲景上

童綜合醫院

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摘要

本院為推廣及提升各種職類醫學繼續教育的有效度，使用結合現代電子網路及互動教學合併之翻轉教學法，以期能加深及加廣教學內容，使學員能將所學真正的應用於臨床工作上，進而提升醫療照護的品質，此教學法不同於傳統教學的地方，在於將傳統課堂上的教學內容及資料，利用錄影帶或相關的教學平台，先行讓學員彈性的使用自己方便的時間及地點學習，而學員們與講師課堂上則是跳脫於傳統授課那種以老師講授為主的教學模式，取而代之的是一種以活動及互動式的教學，此方法的主軸為讓學員自我學習，藉助討論及實際操作，不斷提升能力，落實醫學繼續教育的成效。

關鍵詞：翻轉教學、互動式教學、醫學繼續教育

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Tungs' Medical Journal 9 (2015) 76-83

Review Article

Interventional Cardiac Catheterization for Structural Cardiovascular Defects : The State of the Art in Taiwan

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Abstract

Since the introduction of balloon atrial septostomy by Rashkind and Miller in 1966, interventional cardiac catheterization has been developed for more than 40 years. With the development of new medical equipment, balloon catheters, stents, various occlusion devices, and the advancing imaging modalities, many congenital and acquired structural anomalies of cardiovascular system can be successfully treated without open chest and/or heart. Basic techniques including dilatation and occlusion are performed percutaneously from the peripheral vessels of inguinal regions under general or local anesthesia with sedation. This article reviews the developing skills and current techniques for treatment of structural cardiovascular defects in Taiwan.

Key words: Interventional cardiac catheterization, Balloon catheter, Stent, Coil, Occlusion device

Cardiovascular defect is one of the most common congenital anomalies[1,2]. It is usually presenting with cardiac murmur, cyanosis, symptoms & signs of congestive heart failure and arrhythmias. Besides the adequate medical treatment, surgical correction used to be the standard method and the only choice for complete correction of the cardiovascular anomalies. Cardiovascular sequels, residual lesions after surgery and other acquired abhormalities need usually to do surgical correction. In 1966, Rashkind and Miller described a nonsurgical procedure to create an interatrial communication in infants with d-transposition of great arteries by using a balloon catheter[3,4]. Since then, balloon atrial septostomy is the best choice of palliative therapy for patients with many serious congenital cardiac anomalies, such as d-transposition of great arteries, tricuspid atresia, mitral atresia, and total anomalous pulmonary venous return with a restrictive foramen ovale[1,3-5]. In 1982, Kan J S & Lababidi Z et al used the balloon catheter to dilate the stenotic pulmonary valve to release the pressure gradient[6-8]. Lababidi Z also performed balloon dilatation for the stenotic aortic valve in 1983. Since then, interventional cardiac catheterization became a new area within pediatric cardiology in the 1980s[8-13]. These new method (balloon valvuloplasty) for treating congenital pulmonary and aortic valve stenosis replaced the open valvotomy to become the standard treatment for these particular anomalies[14,15]. With the improvement of quality of balloon, many other lesions with stenotic valves or vessels can also be dilated effectively[1,12,16-19]. The problems of recoil, dissection or rupture of the vessels have been overcome by the introduction of endovascular stents[20]. In the 1990s, many various devices including coils and septal occlude devices were implanted to close ductus arteriosus, unwanted blood vessels, intracardiac and extracardiac communications nonsurgically[15,21-25]. Many different devices had been tried to close the small to moderate size secundum interatrial septal defects (ASD) during the 2000s. In the 2010s, transcatheter closure of interventricular septal defect (VSD) with device and implantation of cardiac valves

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are under clinical trial. In 2007, the Amplatzer Muscular VSD Occluder (AGA Saint Jude Medical Corporation, Plymouth, MN, USA) was approved by the United States Food and Drug Administration (FDA) for transcatheter closure of muscular VSD[26]. This device was also approved by Ministry of Health & Welfare, Taiwan R.O.C in 2009. Without the approval of United States FDA, transcatheter closure of perimembranous and post-infarct VSD with various devices were performed as off-label use.Transcatheter aortic valve implantation (TAVI) has been introduced in Taiwan for the aged patients with severe aortic stenosis. Transcatheter pulmonary valve implantation is under clinical trial in many countries.

Preparation

Interventional cardiac catheterization is usually performed under proper preparation. Although emergency catheterization may be needed in some critical-ill patients, but adequate pre-procedural studies including ECG, trans-thoracic (TTE) or trans-esophageal echocardiography (TEE), chest X-ray and sometimes heart multi-detector computed tomography (CT) and/or MRI imaging are the essential modalities to provide the accurate selection of the types and size of devices and also to monitor the patients during the procedure[27]. Local or general anesthesia and sedation is required. Femoral venous and arterial accesses are routinely needed. Besides the ECG & fluoroscopy, TTE, TEE or intra-cardiac echocardiography (ICE) will provide the best guidance of successful implantation and avoidance of possible complications[1,2,15,28].

Dilatation therapy

Atrial septostomy

Rashkind & Miller introduced the balloon atrial septostomy in 1966[4,5,28]. They created an inter-atrial communication to make the bi-directional shunt at atrial level and to increase the oxygenated blood in systemic circulation which lead to survive the neonate with d-transposition for further surgical correction. This technique also has the benefit in patients with tricuspid atresia, mitral atresia, severe mitral stenosis or insufficiency and total anomalous pulmonary venous return with a restrictive foramen ovale[3-5]. If patient was older than 6 weeks, the atrial septum usually became too thicker to create a defect by balloon, the blade septostomy combined with static balloon dilatation of the atrial septum may be needed to enlarge the inter-atrial communication.

Balloon Valvuloplasty

Since the introduction of balloon dilatation for treatment of valvular pulmonary and aortic stenosis by Kan & Lababidi in 1982[6,7], percutaneous balloon valvuloplasty became the universal acceptance of the best treatment for valvular stenosis. Balloon valvuloplasty is especially useful for the neonates and small infants with critical stenosis to avoid the higher risk of surgery[1,9,14]. In Taiwan, we started to perform the balloon pulmonary valvuloplasty in 1984 at National Taiwan University Hospital (NTUH) and Taipei Veterans General Hospital (TVGH). The indication for intervention is a peak-to-peak systolic pressure gradient over 30 mmHg across the pulmonary valve. For the valvular aortic stenosis, the indication for intervention is excess of 70 mmHg irrespective of the symptoms or a gradient over 50 mmHg with abnormal ST-T changes on ECG or with myocardial ischemic symptoms. In cases of severe or critical stenosis, sequential balloons dilatation starting from a smaller to a bigger balloon can reach the adequate dilatation. If the annulus is too big to allow single balloon catheter for adequate dilatation, double balloons dilatation simultaneously may be needed[14,15]. For the patients of Noonan's syndrome with dysplastic pulmonary valve, surgical valvotomy is usually needed, but transcatheter valvuloplasty with a relatively bigger balloon may be tried. In infants with valvular pulmonary atresia, balloon valvuloplasty can be done after first perforating the atretic valve with a radiofrequency catheter or a hard guidewire. Congenital aortic valvular stenosis in children can usually be treated with balloon dilatation. Avoidance of over-size of balloon for dilatation is necessary to protect from the possible complication of significant aortic regurgitation. In spite of congenital or acquired etiology, balloon dilatation of the stenotic tricuspid valve and mitral valve may also be performed with good results[15].

Balloon Angioplasty

In 1983, Lock JC et al started to perform balloon angioplasty for the hypoplastic and stenotic peripheral pulmonary arteries[16,17]. The previous reports indicated that balloon dilatation of peripheral pulmonary arterial stenosis has about up to 50% successful

results[17,18]. We started to perform balloon angioplasty for the peripheral pulmonary arterial stenosis at NTUH and TVGH since 1988. Besides the peripheral pulmonary arteries stenosis, balloon angioplasty can also dilate other peripheral and central arteries, such as stenotic renal artery, narrowing ascending and descending aorta[5,20]. For the native coarctation of the aorta in neonates and infants, a long segment of narrowing or those associated with hypoplasia of the isthmus or transverse aortic arch, balloon dilatation may carry higher risks of dissection, aneurysmal formation or rupture of the aorta. For the discrete native coarctation and post-surgical re-stenosis, balloon angioplasty is the treatment option in patients with significant hypertension and/or with a pressure gradient over 20 mmHg across the narrowing[1,2,5].

Balloon Dilatation for Other Narrowing Native or Acquired Cardiovascular lesions

In neonates and small infants with cyanotic & complex cardiovascular lesions, total surgical correction cannot be performed either due to younger age, lower body weight or inadequate size of pulmonary arteries, balloon dilatation of the right ventricular outflow tract may replace the surgical aorto-pulmonary shunting procedures as the alternatively palliative treatment. Balloon dilatation can also enlarge the stenotic surgical shunts, conduits and baffles to increase the blood flow as necessary[15].

Endovascular Stent Implantation

The most serious complications of balloon angioplasty are dissection, aneurysmal formation, and rupture of the vessels[12, 29]. Recoil of the vessels due to the elasticity reduced the long-term effect of balloon angioplasty. Those problems have been overcome after the introduction of endovascular stents implantation by Mullins C in 1988[20]. In patients with significant stenosis of peripheral pulmonary arteries and coarctation of the aorta, especially those who have residual stenosis after surgery and the re-do surgery may be disappointing or carry a higher risk, the balloon expandable stents will be the choice in spite of the absence of approval for vascular lesions in children by US FDA. We adopted this particular technique for dilatation of the stenotic peripheral pulmonary arteries at NTUH & TVGH since 2000 as off-label use. We had applied Palmaz balloon-expandable stent (Johnson & Johnson Interventional Systems, Warren, NJ, USA), Palmaz Genesis peripheral stent (Johnson & Johnson Interventional Systems, Warren, NJ, USA), Cheatham-Platinum stents (NuMed,Hopkinton, NY, USA) and IntraStent (ev3 Endovascular Inc. Plymouth, MN, USA) to dilate the stenotic peripheral pulmonary arteries and coarctation of the aorta. To keep up with the child's growth, these stents can be further expanded with a bigger balloon to a proper diameter of the vessels[30-32]. The patients with peripheral pulmonary arterial stenosis after total correction of tetralogy of Fallot and d-transposition of great arteries had been treated well[31]. Gradual dilatation and/or implantation of a covered stent (NuMed,Hopkinton, NY, USA) are required to avoid rupture or formation of an aneurysm in cases of severely stenotic lesions, such as native coarctation of the aorta[30,33]. With the improvement of medical equipment and technique, many various stents including covered stents and biodgradable stent have been developed or under developing. Transcutaneous aortic valve implantation (TAVI) with Edwards SAPIEN XT Transcatheter Heart Valve (Edwards Lifesciences LLC, Irvine, CA, USA) had applied to treat the aged patients with severe calcified aortic valve and higher surgical risk since 2012 in Taiwan. Although Melody Transcatheter Pulmonary Valve (Melody valve, Edwards Lifesciences LLC, Irvine, CA, USA) received Pre-Market approval from the US FDA in February 2015, this particular technique is still undergoing clinical trial in many countries.

Occlusion Therapy

Patent Ductus Arteriosus (PDA)

Closure of a hemodynamically significant PDA is the standard care. For the patients with a small PDA or a silent PDA, closure is also to be considered to avoid the possible complications, such as pulmonary arterial hypertension and endocarditis. In 1967, Portsmann W applied a ivalon foam plastic plug to close the larger PDA [23]. Because of a larger diameter of femoral arterial sheath (18 to 28F) was needed to deliver the ivalon plug, it limited the further development and clinical application. In the following years, many different devices including Rashkind umbrella, detachable balloon, Sideris' device, double umbrella and Amplatzer device had been developed to close the PDA percutaneously[25,34-36]. In 1993, Cambier PA first applied the Gianturco coil (Cook, Bloomington, IN, USA) to close the small PDA with diameter

less than 2.5 mm[37]. We started to use the coil to close small and moderate size PDA at NTUH & TVGH since 1995.Detachable Cook coil & Pfm Nit-Occlud coil (Pfm Medical, Germany) had also been tried in Taiwan for closure of PDA[38]. Multiple coils implantation with different methods had been applied for closure of a larger PDA but with the risk of coil embolization in the peripheral pulmonary arteries or aortic branches[25,39]. Since 1999, Amplatzer Duct Occluder (AGA Saint Jude Medical Corporation, Polymouth,MN, USA) has been introduced to close a larger PDA (narrowest diameter of ductus over 2.5 mm) in Taiwan[40,41]. The surgical risks of PDA include rupture of calcified ductal wall with ageing, recurrent laryngeal nerve injury and other possible complications of anesthesia and open chest surgery. Almost every patient with PDA should be tried to close percutaneously with coil or device, such as Amplatzer Duct Occluder[34,42]. The choice of coil or device is dependent on the narrowest diameter, shape and length of the ductus. Since 2014, Fu YC at Taichung Veterans General Hospital (Taichung VGH) started to transcatheter closure of PDA in the lower birth weight and premature babies who had a significant PDA and did not respond to medical therapy as well as a higher risk for surgical ligation[36,43,44].

Other Native and Acquired Abnormal Vessels and Arteriovenous Fistula or Communications

The coil, vascular plug and other devices can also be applied to close the abnormal small vessels such as major aortopulmonary collateral arteries in extreme tetralogy of Fallot, arteriovenous fistula, and pulmonary sequestration, etc. Collaterals from systemic to pulmonary veins in patients after Glenn or Fontan operations can be occluded with coils or devices. The small coronary arteriovenous fistula, pulmonary arteriovenous fistula, hereditary hemorrhagic telangiectasia with or without symptoms may also need to be closed with the coil, plug or devices.The palliative surgical aorto-pulmonary shunt in patients with complicated cyanotic congenital heart diseases can be closed with coils or devices before the total correction to shorten the operative time and reduce the possible complications of anesthesia and surgery.

Interatrial Septal Defect (ASD)

The anatomical locations of ASD are classified as ostium primum, ostium secundum, sinus venous and coronary sinus septal defect. In 1976, King & Mills reported to successfully close the inter-atrial septal defect at cardiac catheterization laboratory. After that, Rashkind Umbrella Device, Double Umbrella Device, Clamshell Device, CardioSeal Device, StarFlex device (NMT Medical Boston, MA, USA) Angel Wing Device, and Sideris Button Device had been tried but not appreciated as the universal utilization. Until 1997, the development of Amplatzer Septal Occluder (Saint Jude AGA Medical Corporation, Plymouth, MN USA) made the transcatheter closure of ASD easier and as the first choice for non-surgical treatment of secundum ASD[45,46]. Transcatheter closure of ASD has been reported to improve right ventricular function, decrease in cardiac size and also increase in exercise capacity[47]. After the limited clinical experiences with Rashkind Umbrella, Sideris Button Device and CardioSeal Device, we started to apply Amplatzer Septal Occlude as the first choice for transcatheter closure of secundum ASD in Taiwan since 1999. Nowadays, transcatheter closure of secundum ASD with device is the best choice of treatment if the balloon-stretched diameter of the defect is less than 40 mm and with the surrounding rims over 2 mm. The newer Occlutech Figulla Flex II Device (Occlutech GmbH, Jena, Germany) has also been introduced in Taiwan to close ASD since 2014, but only with a limited experience.

Interventricular Septal Defect (VSD)

Interventricular septal defect is the most common type of congenital cardiac defects. It was classified as supracristal, perimembranous, edocardial cushion and muscular types in according to the locations of defect. Surgical correction is used to be the gold standard for total correction in cases of failure to thrive, signs, symptoms of congestive heart failure and pulmonary hypertension. Percutaneous transcatheter closure of VSD was first reported by Lock et al in 1987 by using a Rashkind Umbrella Device. Since then, several devices including Sideris Button Device, Gianturco and detachable coils, Pfm Nit-Occlud, Chinese Symmetric and Asymmetric VSD Occluder (Shanghai Memory Alloy Material Co., Huayishengjie Material Co., Beijing, China) had been tried to close the VSD percutaneously, but without universal acceptance.[49] In 2007, the Amplatzer Muscular VSD Occluder (AGA Medical Corporation, Plymouth, MN, USA) was approved by the United States FDA for transcatheter closure of muscular VSD. This

device was also approved by Ministry of Health & Welfare, Taiwan R.O.C in 2009 to close the muscular VSD. Since the relatively higher incidence of complete atrioventricular block(5-7%) after transcatheter closure of perimembranous VSD by Amplatzer Membranous VSD Occluder, it is still undergoing clinical trial in USA[49-52].

During the last 10 years, many different devices including Amplatzer Duct Occluder, vascular plug, and Amplatzer Duct Occluder II were applied as off-label use to close the perimembranous VSD. This technique had also been introduced to Taiwan by Dr. Fu YC & Wang JK since 2013 for closure of perimembranous and post-infarct VSD. The preliminary experience was exciting and indicating the effective method for closure of perimembranous VSD without the major complications of heart block and/or tricuspid valve injury which were more common in cases with Amplatzer Membranous VSD Occluder.

Complications

As the other invasive procedures, interventional cardiac catheterization carries risks which are dependent on the type of cardiovascular lesions, type of procedures, patients' age and general conditions, and also the operator's experience & technique[52,53]. The major complications were reported as higher as 3-7% in previous literature. The most serious complication of mortality during or immediately after procedure is rare (0.07 to 0.2%) in spite of the age of patients[54]. The most common complications are arrhythmias which including cardiac standstill, severe bradycardia, heart blocks, atrial tachycardia, ventricular arrhythmias, bundle branch block and ST-T wave changes[52-58]. They are usually transient and recovery without sequel. The second most common complication is vascular injury to cause thrombosis, bleeding, aneurysmal formation and fistula. Other relatively uncommon complications include device embolization, catheter-related complications and allergic reactions to drugs or contrast medium. Although most of major complications can be treated medically, but back-up by the cardiovascular surgeon should be needed for the possible emergent cardiovascular rescue surgery.

Conclusion

Transcatheter interventional catheterization is a relatively new method for treatment of structural cardiovascular lesions in Taiwan. It is a safe, feasible and effective method to replace some surgical procedures for many different cardiovascular lesions. The advantages of transcatheter treatment include fewer complications, avoidance of cardiopulmonary bypass and cardioplegia, shorter hospitalization stay, reduced need of blood products, less discomfort and absence of operative scar over chest wall. Many new devices are still undergoing development or clinical trial for cardiovascular anomalies, such as obliteration of left atrial appendage, repair of mitral regurgitation with MitraClip or transcatheter mitral valve implantation etc. In the near future, more and more cardiovascular anomalies can be treated successfully in the catheterization laboratory or operating theater as hybrid procedure. The best cooperation of cardiologist, cardiovascular surgeon, anesthesiologist,nurse and technician should work together to treat the patients with complicating cardiovascular anomalies by using balloons, stents, coils, and/or devices.

Disclosure of Interest

The authors declare that is no conflicts of interest concerning this article.

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介入性心導管術治療結構性心臟血管畸形異常：在台灣的發展及現況

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摘要

自從 1966 年 Rashkind 及 Miller 醫師首創以球囊導管，完成心房中膈造口術，姑息治療大動脈轉位病嬰後，介入性心導管術已發展 40 餘年。由於許多新的醫療儀器開發，球囊導管、支架、各種封堵器的研發及心臟血管影像學的進步，使許多先天性及結構性心臟血管的畸形異常，都可經不剖開胸腔及（或）不剖開心臟手術而治（療）癒。介入性心導管擴張術及關閉術都是在全身或局部麻醉或鎮靜劑的協助下，經皮穿刺，由腹股溝處動靜脈，將導管、支架、或各種封堵器置入，就可完成手術。

本篇是介紹在台灣，這種介入性心導管術治療結構性心血管缺損的發展及目前現況。

關鍵詞：介入性心導管術、球囊導管、支架、彈簧圈、封堵器

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Original Article

Cholecystokinin Type A Receptor Expression is Correlated with Poor Survival in Patients with Colon Cancer

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Abstract

Background and purpose: Cholecystokinin (CCK) and the gastrin receptors, CCKAR and CCKBR, are overexpressed in different malignancies of the human digestive tract; however, limited information is available regarding the correlation of their expression in colon cancer. The present study aimed to investigate whether the levels of expression of CCKAR and CCKBR were associated with the clinicopathological features of patients with colon cancer.
Methods: CCKAR and CCKBR expression levels were determined using immunohistochemical analysis. Samples obtained from 49 surgical specimens were used for pathological examinations.
Results: Cytoplasmic and nuclear staining of CCKAR was detected in 78% and 49% of samples, respectively, and did not correlate with the patients' sex, tumor grade, or stage of tumor progression. However, strong nuclear, but not cytoplasmic, staining of CCKAR was significantly associated with relatively poor 1-year survival (P = 0.032). In contrast to CCKAR, weak to moderate staining of cytoplasmic CCKBR was detected in 84% of samples. Further, CCKBR stained weakly in the nucleus. Cytoplasmic CCKBR correlated only to the stage of tumor progression (P = 0.048). There was no significant association of nuclear CCKBR expression with patients' clinicopathological characteristics.
Conclusions: Our results show that cytoplasmic CCKBR expression and nuclear CCKAR expression were associated with the stage of tumor progression and 1-year survival, respectively. These findings suggest that CCKAR could serve as a potential marker for poor prognosis of patients with colon cancer and may play an unknown role in colon carcinogenesis.

Key words: Cholecystokinin type A receptor, Cholecystokinin type B receptor, colon cancer, 1-year survival

Introduction

Colon cancer is one of the most common malignancies worldwide. In the United States, approximately 6% of individuals will develop this malignancy during their lifetime, and 50% of these patients will die from this disease. The risk of developing colon cancer is influenced by environmental and genetic factors [1]. In general, the colon cancer incidence rises in parallel with economic development, with the majority of cases occurring in industrialized countries because the disease is strongly associated with a Western lifestyle. Risk factors associated with colon cancer development include obesity [2], high red meat consumption [3], and alcohol abuse [4].

Cholecystokinin (CCK) and gastrin regulate digestive functions and stimulate the proliferation of normal and of neoplastic cells [5,6]. Indeed, patients presenting with a gastrinoma often exhibit hypertrophy of the gastric mucosa and hyperplasia of acid-secreting parietal cells and enterochromaffin-like cells [5,6]. Moreover, the growth of numerous cancer cell lines derived from gastric, colorectal, pancreatic, and bronchogenic carcinomas can be stimulated by gastrin or inhibited by antagonists of the CCK and gastrin receptors [5,6]. Notably, gastrin peptides are detected in several digestive cancers as well as other cancers such as thyroid cancer and astrocytic tumor, suggesting that autocrine regulation of the growth of

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these neoplastic cells occurs when functional CCKB/gastrin receptors are present [6,7].

Compared with studies of the correlation of the expression and function of CCKB/gastrin and their receptors in digestive tumors, few studies are available regarding the CCK type A receptor (CCKAR). For example, the expression of the mRNA encoding CCKAR was detected in 62.5% of esophageal cancers and 41.7% of colon cancers compared with 0% and 16.7% detection, respectively, of CCKBR [8]. Furthermore, antagonism of CCKAR, but not CCKBR, inhibits the proliferation of the colon cancer cell line HT-29[9]. However, the correlation between expression and intracellular localization of CCKAR and CCKBR with patients' clinical features remains unclear.

In the present study, we aimed to determine whether the expression and localization of CCKAR and CCKBR were associated with specific clinicopathological features of patients with colon cancer in Taiwan.

Materials and Methods

Sample collection

Forty-nine formalin-fixed and paraffin-embedded colon cancer specimens were obtained from patients who underwent surgical resection at the Department of Surgery of Tungs' Taichung MetroHarbor Hospital (Taichung, Taiwan) from 1999 to 2008, and tissue blocks were obtained from Department of Pathology of the same hospital. Tumor stages and grades were classified according to the TNM and World Health Organization classification systems. Histopathological and clinical data were obtained from the cancer registry of Tungs' Taichung MetroHarbor Hospital. Disease-free survival was measured as the time between the surgery and either the date of death or the end of follow-up. The internal review board of Tungs' Taichung MetroHarbor Hospital approved this study.

Immunohistochemical (IHC) analysis of the level of CCKAR expression in the nucleus

IHC analysis was performed using a streptavidin-peroxidase protocol. Briefly, 4-μm-thick sections of paraffin-embedded cancer tissue and paired noncancerous tissue were deparaffinized. After blocking with 3% hydrogen peroxide, the sections were rehydrated; then, the antigen was exposed by heating at 100°C for 20 min in 10 mM citrate buffer (pH 6.0). After incubation with antibodies against CCKAR and CCKBR [1:70 dilution, rabbit polyclonals (ab28627 and ab183124), Abcam, UK] for 20 min at room temperature, the sections were washed with PBS and then incubated with peroxidase-conjugated secondary antibodies (Santa Cruz Biotechnology, Santa Cruz, CA, USA) for 30 min. Antibody-antigen complexes were detected using 3,3'-diaminobenzidine tetrahydrochloride and counterstained with hematoxylin. Appropriate positive and negative controls were also prepared. After staining, the prepared slides were scored by two pathologists. Paraffin-embedded and fresh-frozen sections of normal colonic epithelium of a subject with a homogeneous immunophenotype for the respective antigens were included as positive controls. Samples reacted with secondary antibody alone were used as negative controls. The intensity of IHC staining was scored semi-quantitatively according to the percentage of positive cells in individual lesions, ranging from 0 to 4, as described previously[10]. The intensity was classified as either weak (<2) or strong (≥2).

Statistical analysis

Statistical analysis was performed using SPSS software (SPSS, Inc., Cary, NC). The correlation between the expression levels of tumors with different clinicopathological characteristics was evaluated using the Chi-square and the Fisher's exact tests. $P < 0.05$ was considered statistically significant.

Results

Patient characteristics

Table 1 shows the clinicopathological data of 49 patients [21 men (57.1%) and 28 women (42.9%)] with colon cancer aging 24-96 years (median 63.1 years). Histopathological analysis revealed that 6, 20, and 23 patients had well, moderately, and poorly differentiated tumors, respectively, and that tumor stages of 14, 14, 11, and 10 patients were T1, T2, T3, and T4, respectively. The 1-year survival rate of the 49 patients was 69.4%.

Correlation of cytoplasmic staining of CCKAR and CCKBR with the clinicopathological parameters of patients with colon cancer

CCKAR and CCKBR are reportedly involved in human tumorigenesis[10,11]. Therefore, we

investigated whether there was a correlation between the expression levels of CCKAR and CCKBR and clinicopathological characteristics of patients with colon cancer. For this purpose, we conducted IHC analyses of the cytoplasmic levels of CCKAR and CCKBR in samples from 49 patients with colon cancer as described above. Cytoplasmic staining and nuclear staining were detected in the cytoplasm and nucleus of 95.9% and 93.9% of tumor samples, respectively (Fig. 1). Weak cytoplasmic staining (<1) of CCKARA was detected in approximately 22.4% of tumor samples. In contrast, cytoplasmic and nuclear staining of CCKBR was detected in 93.6% and 20.6% of tumor samples, respectively (Fig. 2). Weak cytoplasmic staining and weak nuclear staining (<1 or 0) of CCKBR were detected in approximately 73.5% and 65.3% of tumor samples, respectively (Fig. 2). The correlation between the cytoplasmic staining of CCKAR and CCKBR and clinical parameters is summarized in Table 2, and the results show that cytoplasmic staining of CCKAR and CCKBR was not significantly associated with the sex, histological differentiation, or 1-year survival. Notably, cytoplasmic staining of CCKBR, but not CCKAR, was significantly correlated with the stage of tumor progression (P = 0.048).

Table 1. Clinicopathological characteristics of the patients

Characteristic	Number	%
Total patients	49	100
Median age (range)	63.1 (24 to 96)	
Gender		
Female	21	42.9
Male	28	57.1
Histologic appearance		
Well differentiated	6	12.2
Moderately differentiated	20	40.8
Poorly differentiated	23	47.0
T stage		
T1	14	28.6
T2	14	28.6
T3	11	22.4
T4	10	20.4
Survival duration		
≤1	15	30.6
>1	34	69.4

Correlation of nuclear staining of CCKAR and CCKBR with clinicopathological characteristics of patients with colon cancer

Nuclear staining of CCKAR was not significantly associated with sex, histological differentiation, or stage of tumor progression (Table 3). Notably, nuclear staining of CCKAR was significantly elevated and was associated with worse 1-year survival (P = 0.032; Table 3). In contrast to detection of CCKAR in the nucleus,

Table 2. Clinicopathological characteristics of patients and cytoplasmic staining of CCKAR and CCKBR protein

	cytoCCKAR staining			cytoCCKBR staining		
	<2 (n=11)	≥2 (n=38)	*P* value	<2 (n=36)	=2 (n=13)	*P* value
Gender						
Female	5	16	1.000	13	8	1.000
Male	6	22		23	5	
Histologic appearance						
Well/moderately	6	20	1.000	20	6	0.747
Poorly	5	18		16	7	
Stage						
T1/T2	8	20	0.311	24	4	0.048*
T3/T4	3	18		12	9	
Survival						
≤1 year	4	11	0.716	10	5	0.500
>1 year	7	27		26	8	

cyto, cytoplasmic. * Statistically significant.

nuclear expression of CCKBR was not significantly associated with any of the variables analyzed. Moreover, nuclear expression of CCKBR was not detected in the tumor samples from patients who survived less than 1 year after diagnosis of colon cancer.

Discussion

Colon cancer is a leading cause of cancer-related deaths, and its prevalence in Taiwan has markedly increased in the past decade. The increased prevalence and mortality of patients with colon cancer may be associated with Western-style diets and the ensuing metabolic syndrome that may arise. The gastrointestinal peptide gastrin promotes the growth of multiple malignancies, including cancers of the colon

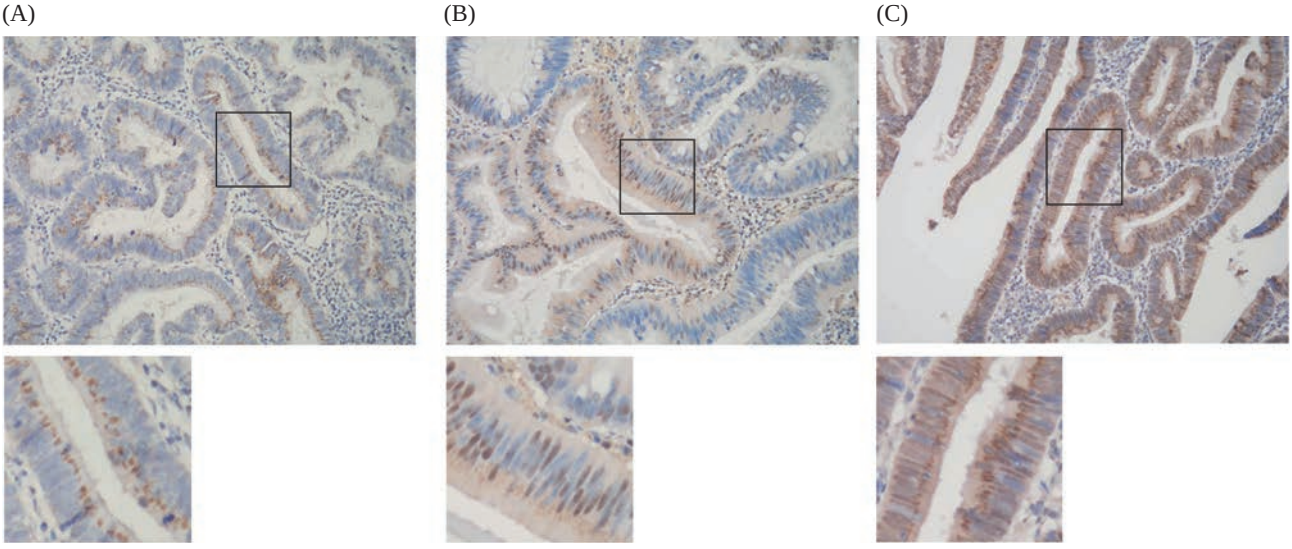

Fig. 1 Immunohistochemical staining for the expression of CCKAR in colon carcinomas. The staining patterns of CCKAR were (A) predominantly cytoplasmic, (B) mixed cytoplasmic and nuclear, and (C) predominantly nuclear. (A) and (B) for moderate staining and (C) for strong staining. Both cytoplasmic and nuclear CCKAR were not detected in non-tumor part of colon carcinomas.

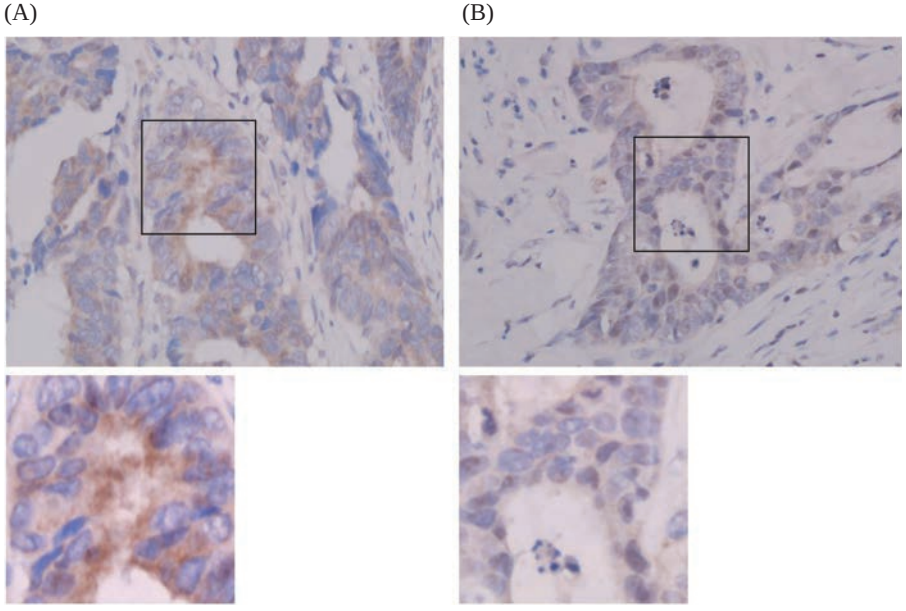

Fig. 2 Immunohistochemical staining for the expression of CCKBR in colon carcinomas. The staining patterns of CCKBR were (A) moderately cytoplasmic and negatively nuclear (B) weakly cytoplasmic and negatively nuclear. Both cytoplasmic and nuclear CCKBR were not de

Table 3. Clinicopathological characteristics of patients and nuclear staining of CCKAR and CCKBR protein

	nuCCKAR staining			nuCCKBR staining		
	<2 (n=25)	≥2 (n=24)	*P* value	=0 (n=32)	=1 (n=17)	*P* value
Gender						
Female	8	13	0.154	17	4	0.070
Male	17	11		15	13	
Grade						
Well/moderately	16	10	0.156	14	10	0.377
Poorly	9	14		18	7	
Stage						
T1/T2	14	14	1.000	22	8	0.218
T3/T4	11	10		10	9	
Survival						
≤1 year	4	11	0.032*	0	0	1.000
>1 year	21	13		32	17	

nu, nuclear. * Statistically significant.

[12], stomach [13], lung [14], and pancreas [15].

There are multiple isoforms of CCK receptors [16,17]. Among them, CCKAR (CCK1R) binds cholecystokinin with the highest affinity [18], and the CCKBR receptor (CCK2R) binds cholecystokinin and gastrin with equal affinities [19]. The CCKAR and CCKBR belong to a family of guanosine triphosphate-coupled receptors containing seven-transmembrane domains [19]; however, the biological functions of the two CCK receptors are not identical. For example, Harikumar *et al.* reported that stimulus-activity coupling through CCKAR, but not CCKBR, is affected by cholesterol [20], and González-Puga *et al.* demonstrated that only CCKAR antagonists inhibit the proliferation of HT-29 [9]. Recent studies show that gastrin expression correlates with adenomatous polyposis and promotes intestinal polyposis via CCKBR-mediated signaling and that a mutant CCKBR with increased activity enhances tumorigenesis of colorectal cancers, implicating gastrin/CCKBR in the development of colorectal cancers [21-23]. Furthermore, our results indicate that cytoplasmic staining of CCKBR is associated with the stage of tumor progression.

CCKAR and CCKBR are differentially expressed in three human tumors, indicating that the expression in esophageal and colorectal cancers but not in stomach cancer of the mRNA encoding CCKAR is higher compared with that of CCKBR [8]. These findings are consistent with those of the present study, which reveal that cytoplasmic and nuclear staining of CCKAR was higher compared with that of CCKBR, suggesting that CCKAR was highly expressed in colon tumors. Moreover, CCKAR is detected in human cancers such as pancreatic cancer [8,24,25]. However, further information regarding CCKAR expression and the clinical outcomes of patients with colon cancer is limited. The present study explored the correlation between cytoplasmic and nuclear staining of CCKAR and CCKBR and the clinicopathological features of patients with colon cancer; the results reveal that only nuclear staining of CCKAR was associated with poor 1-year survival. However, more tumor samples with clinicopathological characteristics are required to further evaluate the roles of CCKAR in colon carcinogenesis.

The present study demonstrated that nuclear, but not cytoplasmic, staining of CCKAR was associated with poor 1-year survival. Moreover, nuclear, but not cytoplasmic, staining of CCKAR appears to be associated with metastasis of colon cancer and other malignancies (data not shown). In contrast, nuclear staining of CCKBR was observed infrequently in the present study. Taken together, these findings indicate that CCKAR present in the nucleus may serve as a marker for poor prognosis of patients with colon cancer. Moreover, the present findings suggest nuclear translocation of CCKAR may play an unknown but pivotal role in the progression of colon carcinoma

as well as in metastasis. Further *in vitro* and *in vivo* studies are required to explore the tumorigenic roles of nuclear CCKAR and the underlying molecular mechanisms.

In conclusion, the present study is the first to demonstrate that nuclear staining of CCKAR is associated with poor 1-year survival in patients with colon cancer.

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膽囊收縮素 A 型接受器的表現與大腸癌患者生存率的相關性

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摘要

背景與目的：膽囊收縮素 A 型接受器（CCKAR）已知在不同的惡性腫瘤中有過度表現的報告，但是對於此一過度表現與大腸癌之間關係的了解仍相當有限。因此，本研究擬針對膽囊收縮素 A 型接受器在大腸腫瘤組織中的表現，與大腸癌患者的存活率進行探討。
實驗方法：利用免疫組織染色法，進行從 49 為大腸癌患者切除下來的剩餘檢體，進行膽囊收縮素 A 型接受器的定性與半定量分析。同時搭配其臨床資料進行相關性的統計分析。
實驗結果：本研究結果顯示，膽囊收縮素 A 型接受器在細胞質與細胞核的表現，與大腸癌患者的性別、腫瘤分期與病程進展無顯著意義。但是膽囊收縮素 A 型接受器在細胞核的表現卻與患者一年存活率有顯著相關（P=0.032），核染色的表現越強，一年存活率越低。
研究結論：本研究首次發現膽囊收縮素 A 型接受器會轉移到細胞核，且核染色越強其一年存活率越差。這些研究結果暗示著膽囊收縮素 A 型接受器在大腸腫瘤癌化的過程中，可能扮演著重要且未知的角色。

關鍵詞：膽囊收縮素 A 型接受器、大腸癌、一年存活率

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Original Article

Prevalence of and Factors Associated with Colorectal Neoplastic Polyps and Sporadic Hyperplastic Polyps in a Self-paid Colonoscopy Population

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Abstract

Background and purpose: Current colonoscopy screening strategies suggest providing the same management for patients with small or few sporadic hyperplastic polyps and a negative history of colorectal neoplastic polyps and for patients without polyps. This study aimed to investigate the presence of differences in clinical characteristics among the three patient populations (i.e., neoplastic polyp, hyperplastic polyp, and non-polyp), as well as the prevalence of and factors associated with colon neoplastic polyps and sporadic hyperplastic polyps in an asymptomatic population.
Methods: A retrospective cross-sectional study of 755 cases was conducted. All patients underwent full colonoscopies in participating the self-paid health examination programs at a regional hospital from January to September 2009. Data regarding demographics, common addictive substance use, biochemical measurements, comorbidities, and pathologic diagnoses of detected lesions were obtained via medical chart review. Diagnosed cases were accordingly classified as neoplastic polyps, hyperplastic polyps, or controls.
Results: The overall prevalence of neoplastic and hyperplastic polyps were 9.5% and 7.4%, respectively, and were higher among men. Patients in both lesion groups were similar with respect to most characteristics, and lesions were associated with smoking, older age, and a high body mass index (BMI). After adjusting for the aforementioned three factors, cases with hyperplastic polyps tended to have higher uric acid levels compared with controls (odds ratio = 1.21, 95% confidence interval: 1.01-1.45, p = 0.036).
Discussion: This study examined the epidemiologic characteristics of two types of colorectal lesions in a domestic population using data from a self-paid health examination database, which resembles an asymptomatic population. The results illustrated that both types of lesions were associated with common colorectal cancer risk factors (smoking, age, and BMI), and those with hyperplastic polyps differed from the controls. Therefore, cases with hyperplastic polyps should not be treated as polyp-free ones, while the prognosis differences between the two types of lesions will depend on further studies.

Key words: Colonoscopy, Neoplastic polyps, Hyperplastic polyps

Introduction

Colorectal adenoma has long been recognized as a precursor of colorectal neoplasia[1]. Hyperplastic polyps can develop as sporadic hyperplastic polyps and hyperplastic polyposis syndrome, a rare condition characterized by multiple large hyperplastic polyps throughout the colon; this condition is highly coexistent with neoplastic polyps, including serrated adenomas, in the proximal colon. In recent decades, many studies have attempted to distinguish these categories of hyperplastic polyps and findings have indicated that only those occurring with hyperplastic polyposis syndrome have significant neoplastic potential[2-5].

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Current colonoscopy screening strategies grade patients with small or few hyperplastic polyps and no history (personal or close family) of colorectal neoplasms as average-risk, suggesting that they should be managed in the same manner as patients without polyps. As a result, clinicians often downplay the observations of hyperplastic polyps in an average-risk population. However, even if such observations were noted in colonoscopy reports, the available information (e.g., prevalence, genesis, perpetuation, progression, or related factors) that could be provided to patients is limited.

Serrated polyps, or microscopic features of mixed tubular adenomas and hyperplastic polyps, were once considered non-neoplastic [1,6]. However, studies of symptomatic or high-risk populations suggested that these hyperplastic polyps were significant markers of synchronous adenomas or colorectal cancer [7,8], and morphologic analysis suggested that multiple, large, and proximally located hyperplastic polyps might develop into neoplasms [2]. These findings reignited researchers' interest in the identification and classification of hyperplastic polyps in recent decades [3,9], and similar results have been observed in large-scale colonoscopy screening studies involving asymptomatic populations [4,10]. Recently, researchers reached a consensus that sessile serrated adenomas (SSA) and traditional serrated adenomas (TSA) are also neoplastic because mixed hyperplastic polyp and tubular adenoma could develop a neoplastic polyp pathway, and these lesions should therefore be followed intensively [5].

Investigations of the factors associated with neoplastic polyps are understandably important in the field of colorectal cancer prevention, particularly with regard to the development of high-risk population screening strategies. Although many studies have investigated the epidemiology of colorectal neoplastic polyps, few have addressed sporadic hyperplastic polyps [11-13]; the latter accounts for the largest proportion of clinically observed lesions, yet medical/professional societies do not currently recommend that these lesions receive continuing surveillance. This lack of recommendation largely depends on western practice guidelines; such cases are considered to be polyp-free.

To date, no domestic evidence supports the assertion that the epidemiologic features of a population with sporadic hyperplastic polyps resemble those of a polyp-free population. Moreover, most clinical colorectal cancer cases occur sporadically in average-risk individuals with no family history [14,15]. In this preliminary study, the prevalence of and factors associated with both neoplastic and sporadic hyperplastic polyps were simultaneously investigated to better understand the related comorbidities and characteristics of patients with such lesions in a domestic population.

Materials and Methods

Study design and population

This study retrospectively reviewed the medical records of patients who had undergone full colonoscopies through self-paid health examination programs from January 1 to September 30, 2009 at Tung's Taichung MetroHarbor Hospital (TTMHH), a regional hospital in coastal central Taiwan. Two colonoscopes (Olympus CF240L; Olympus Corporation, Shinjuku, Tokyo, Japan) were used for the examinations. All examinations to determine polyp sizes and morphologic characteristics were performed and recorded by the same gastrointestinal physician. A medical technologist supervised the medical chart reviews and study dataset creation. The neoplastic polyp group (polyps with mild, moderate, or severe dysplasia or carcinomatous changes) included subjects with a pathologic diagnosis of tubular adenoma (adenomatous polyps), villous adenoma, tubulovillous adenoma, or serrated adenoma. The non-neoplastic polyp group (polyps without dysplastic changes) included subjects with a pathologic diagnosis of hyperplastic polyps, inflammatory polyps, or juvenile polyps. This study was approved by the Institute Review Board of TTMHH.

Colonoscopy and biochemical tests

All subjects fasted for at least 8 hours and received midazolam (Dormicum® 5 mg/ml) or meperidine (Demerol 50 mg/ml) intravenously for minor conscious sedation before the examination. The instructions for pre-examination preparation were sent to all participants 1 week prior to the scheduled visit. Subjects whose bowel cleansing preparations were insufficient were excluded from the study participant selection. The common procedures performed by the examination service included anthropometric measurements, blood, urine, and stool specimen biochemical tests,

and a questionnaire-based interview. The questionnaire collected information regarding participants' demographic data, disease history (cancer or chronic disease), family cancer history, and habitual medication usage. The biochemical test report included the levels of hemoglobin (Hb), fasting blood sugar (FBS), aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (Alk-P), total protein (TP), albumin, globulin, triglyceride (TG), serum total cholesterol, lactate dehydrogenase (LDH), blood urea nitrogen (BUN), creatinine (Cr), uric acid, low-density lipoprotein-cholesterol (LDL-C), and high-density lipoprotein-cholesterol (HDL-C).

Statistical analysis

Descriptive statistics (mean, standard deviation, frequency, or percentage) were used to express the sample characteristics. A bar chart was used to illustrate the estimated gender- and age-specific prevalence rates of both types of polyps. Chi-square tests for the contingency table, Fisher's exact test, and logistic regression were applied as appropriate to perform inferential statistical analyses. For multiple logistic regression analyses, stepwise selection was performed with the entry and stay criterion of a p-value <0.2. A significance level of 0.05 was used to indicate a statistically significant association throughout this report. All analyses were performed using SAS 9.1 for Windows (SAS Institute, Inc., Cary, NC, USA).

Results

This study included 755 subjects, of which 59.1% were male. The mean age was 48.69 years (range, 19–88 years). A total of 72 subjects were found to have neoplastic polyps, including 7 (9.72%) with serrated adenomas and mild dysplasia and 65 (90.28%) with tubular adenomas; 56 patients were classified as having sporadic hyperplastic polyps. Another 627 subjects had neither type of polyp (controls).

The overall prevalence rates in this colonoscopy population were 9.5% for neoplastic polyps and 7.4% for hyperplastic polyps; the respective rates of 12.1% and 8.3% among male subjects were higher than the rates of 5.8% and 6.1% among female subjects. The prevalence was also found to increase with age (for detailed estimates, please refer to Figure 1) with a considerable increase in the prevalence of hyperplastic polyps among subjects older than 50 years. This was comparable to the colon cancer distribution reported by the Health Promotion Administration.

Among the 755 subjects, 196 self-reported as regular smokers, 319 as habitual alcohol drinkers, and 57 as betel nut users. Additionally, 24.2% of subjects reported a family history of cancer. Comorbidities among the subjects included hyperlipidemia (n = 185, 24.5%), hypertriglyceridemia (n = 160, 21.2%), hypertension (n = 136, 18.0%), diabetes mellitus (DM) (n = 43, 5.7%), heart disease or arrhythmia (n = 102, 13.5%), asthma (n = 12, 1.6%), osteoporosis (n = 87,

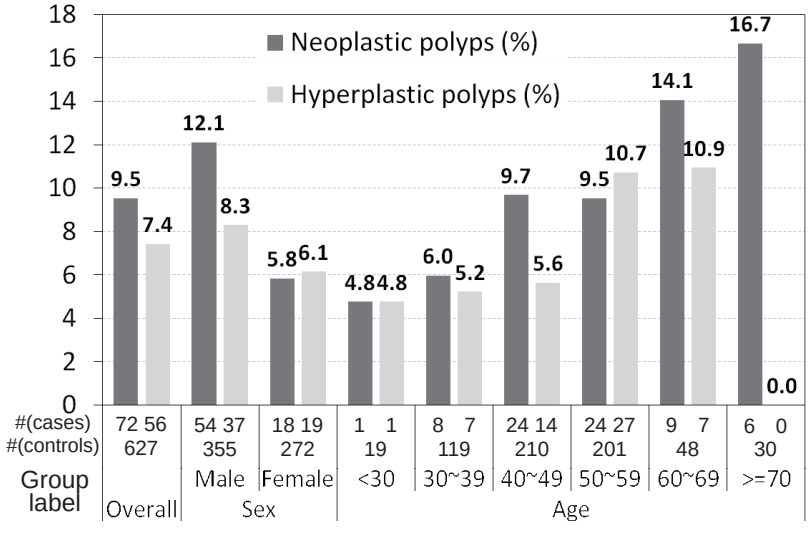

Fig. 1 Sex- and Age-Specific Prevalence of Neoplastic Polyps and Hyperplastic Polyps among Colonoscopy Examination Population. The numbers at the first row below the bars were subgroup case numbers; those at the second row were numbers of controls. The subgroup prevalence was indicated on the top of each bar.

Table 1. The characteristics of the sample.

Groups	Controls		Neoplastic polyps			Hyperplastic polyps		
Variables	*n*	(%)	*n*	(%)	*p-value*	*n*	(%)	*p-value*
	627		72			56		
Gender								
Male	355	(79.6 %)	54	(13.2 %)	0.0027*	37	(9.44%)	0.1705
Female	272	(88.03%)	18	(6.21%)		19	(6.53%)	
Cigarette smoking								
User	145	(73.98%)	31	(17.61%)	0.0004*	20	(12.12%)	0.0451*
No	468	(85.87%)	41	(8.06%)		36	(7.14%)	
Alcohol drinking								
User	246	(77.12%)	44	(15.17%)	0.0007*	29	(10.55%)	0.1177
No	354	(86.76%)	27	(7.09%)		29	(7.09%)	
Betel nut chewing								
User	46	(80.7 %)	9	(16.36%)	0.1292	2	(4.17%)	0.4163†
No	567	(83.02%)	62	(9.86%)		54	(8.7 %)	
Family history of cancer								
Yes	151	(82.51%)	19	(11.18%)	0.6542	13	(7.93%)	0.9812
No	476	(83.22%)	53	(10.02%)		43	(8.29%)	
Comorbidity, present vs. none								
Hyperlipidemia	154	(83.24%)	18	(10.47%)	0.9348	13	(7.78%)	0.8222
Hypertriglyceridemia	129	(80.63%)	21	(14 %)	0.0926	10	(7.19%)	0.6285
Hypertension	108	(79.41%)	17	(13.6 %)	0.1805	11	(9.24%)	0.6476
Diabetes mellitus	28	(65.12%)	11	(28.21%)	0.0002*	4	(12.5 %)	0.3234†
Heart disease/Arrhythmia	82	(80.39%)	11	(11.83%)	0.6027	9	(9.89%)	0.5277
Asthma	9	(75 %)	3	(25 %)	0.0911†	0	(0 %)	1. †
Osteoporosis	73	(83.91%)	8	(9.88%)	0.8938	6	(7.59%)	0.8351
Anemia, yes vs. no	44	(95.65%)	0	(0 %)	0.0171*†	2	(4.35%)	0.5736†
Kidney disease	8	(72.73%)	3	(27.27%)	0.0945†	0	(0 %)	1†
				Mean ± SD				
Age (yrs)	627	48.15 ± 11.04	72	51.79 ± 11.29	0.0083*	56	50.71 ± 8.99	0.0915
Height (cm)	613	163.75 ± 8.5	72	165.11 ± 7.57	0.1935	56	165.40 ± 7.91	0.1636
Weight (Kg)	613	64.6 ± 11.69	72	69.79 ± 11.47	0.0004*	56	68.77 ± 11.29	0.0106*
BMI (Kg/m^2)	613	24 ± 3.32	72	25.52 ± 3.29	0.0002*	56	25.14 ± 3.78	0.0153*
FBS (mg/dl)	624	97.6 ± 29.7	71	108.87 ± 41.03	0.0272*	56	97.73 ± 18.32	0.96
AST (IU/L)	625	28.03 ± 16.99	71	28.65 ± 16.53	0.7712	56	28.46 ± 13.85	0.8528
ALT (IU/L)	625	32.9 ± 33	71	33.76 ± 24.44	0.7875	56	34.93 ± 29.37	0.6568
Alkaline phosphatase (IU/L)	625	61.22 ± 23.61	71	59.86 ± 16.66	0.536	56	61.38 ± 18.32	0.9528
Total protein (g/dl)	625	7.63 ± 0.46	71	7.61 ± 0.48	0.6891	56	7.68 ± 0.47	0.5087
Albumin (g/dl)	625	4.56 ± 0.27	71	4.57 ± 0.31	0.7707	56	4.56 ± 0.3	0.9692
Globulin (g/dl)	621	3.08 ± 0.37	70	3.03 ± 0.41	0.3229	55	3.11 ± 0.4	0.4984

Table 1. Continued

Groups	Controls		Neoplastic polyps			Hyperplastic polyps		
Variables	*n*	(%)	*n*	(%)	*p-value*	*n*	(%)	*p-value*
Triglyceride (mg/dl)	625	151.83 ± 111.81	71	153.2 ± 87.07	0.9034	56	162.23 ± 125.22	0.5093
Cholesterol (mg/dl)	625	197.63 ± 37.5	71	189.13 ± 37.28	0.0706	56	196.73 ± 34.73	0.8634
Lactate dehydrogenase (U/L)	515	107.18 ± 29.63	61	117.07 ± 51.39	0.1455	48	108.35 ± 28.59	0.7928
Blood urea nitrogen (mg/dl)	625	11.63 ± 3.57	71	12.77 ± 3.79	0.0113*	56	11.90 ± 3.26	0.5811
Creatinine (mg/dl)	625	0.96 ± 0.22	71	1.04 ± 0.29	0.0302*	56	1.03 ± 0.21	0.0165*
Uric acid (mg/dl)	625	6.13 ± 1.6	71	6.67 ± 1.6	0.007 *	56	6.79 ± 1.8	0.0034*
LDL-C	622	116.84 ± 33.91	70	110.79 ± 32.42	0.1554	56	116.84 ± 35.25	1
HDL-C	622	52.64 ± 14.53	70	48.73 ± 12.1	0.0304*	56	50.18 ± 14.24	0.2242

Note: the percentages in controls column indicate the proportions of controls in all the subjects; those in neoplastic polyp and hyperplastic polyp columns indicate the proportions of cases in subjects without another polyps. FBS: fasting blood sugar. AST: aspartate aminotransferase. ALT: alamine aminotransferase. LDL-C: the ratio of low dense lipoprotein to cholesterol. HDL-C: the ratio of high dense lipoprotein to cholesterol. *: P-value of less than 0.05 as compared to controls. †: Fisher's exact test was applied.

11.5%), anemia (n = 46, 6.1%), and kidney disease (n = 11, 1.5%). The descriptive statistics of all above-mentioned characteristics and other anthropometric and biochemical measurements are displayed according to diagnosis (i.e., control, neoplastic polyps, and hyperplastic polyps) in Table 1.

Subjects with ascertained neoplastic polyps had the following rates of comorbid diseases: 25%, hyperlipidemia; 29.17%, hypertriglyceridemia; 23.61%, hypertension; 15.28%, DM; 15.28%, heart disease/arrhythmia; 4.17%, asthma; 11.11%, osteoporosis; 0%, anemia; and 4.17%, kidney disease. Among subjects with non-neoplastic hyperplastic polyps, the following comorbidity rates were observed: 23.21%, hyperlipidemia; 17.86%, hypertriglyceridemia; 19.64%, hypertension; 7.14%, DM; 16.07%, heart disease/arrhythmia; 0%, asthma; 10.71%, osteoporosis; 3.57%, anemia; and 0%, kidney disease. The corresponding rates of comorbidities among controls were 24.56%, 20.57%, 17.22%, 13.72%, 4.47%, 13.08%, 1.44%, 11.64%, 7.02%, and 1.28%, respectively. Association analyses of contingency tables revealed significant associations of DM and anemia with the prevalence of neoplastic polyps (p = 0.0002 and 0.0171, respectively), whereas no significant associations were observed between any comorbidity and the prevalence of hyperplastic polyps.

Subjects with a higher prevalence of neoplastic polyps tended to be male, smokers, habitual drinkers, and older relative to the controls. These subjects also had a significantly higher body weight and BMI and levels of FBS, BUN, Cr, and uric acid, as well as lower levels of total cholesterol and HDL-C. Subjects with a higher prevalence of hyperplastic polys also tended to be smokers and older relative to controls, and a significantly higher body weight, BMI, and levels of Cr and uric acid were also observed in these subjects. The relevant summary statistics and associated p-values for all covariates are listed in Table 1.

When subjects with neoplastic and hyperplastic polyps were compared, the former was slightly more likely to use betel nuts (9% vs. 2%, p = 0.0701) and had a higher hypertriglyceridemia rate (29.17% vs. 17.86%, p = 0.1384) and FBS level (108.87 ± 41.03 vs. 97.73 ± 18.32, p = 0.0435). No significant differences between the groups were observed in any other characteristic. The numbers of both polyps did not differ significantly, whereas neoplastic polyps were significantly larger in size than hyperplastic polyps (Table 2). This result was partly related to a belief that only large, serrated growths require further pathological examination. In addition, it is usually not possible to obtain biopsies of tiny luminal growths that are sufficiently large for further pathological examination.

The results of an age-, BMI-, and smoking-adjusted logistic regression analysis of the risks of both types of polyps with respect to controls are shown in Table 3. A high risk of neoplastic polyps was associated with habitual alcohol consumption, high FBS, and asthma, whereas the cholesterol level had a negative effect on the risk. A high risk of hyperplastic polyps was associated with a high uric acid level,

whereas hypertriglyceridemia was found to have a negative effect on the risk. Table 3 lists the associated odds ratio (OR) and 95% confidence interval (CI) estimates. Given the power insufficiency due to the limited sample size, covariates with p-values <0.2 and significant increments in goodness-of-fit of logistic models were presented in the final models.

Discussion

This study explored the prevalence of and factors associated with colorectal neoplastic polyps and sporadic hyperplastic polyps in a population of adults who underwent full colonoscopy exams through a self-paid health examination program. The investigated factors included demographic data, health behaviors, biochemical variables, and comorbidity statuses. Both types of investigated colorectal lesions were more common among men and older subjects, in accordance with the nationwide colorectal cancer distributions reported annually by the authorities. The study results further suggested that smoking and obesity (i.e., high BMI) affect the development of both types of lesions, whereas other factors associated with colorectal neoplasia, such as alcohol consumption, DM, anemia, FBS, BUN, and HDL-C, had no effect on the prevalence of hyperplastic polyps. After adjusting for smoking, age, and BMI, hypertriglyceridemia and a low uric acid level were associated with a low risk of sporadic hyperplastic polyps. This study therefore provided an opportunity to understand the epidemiology of colorectal neoplastic polyps and sporadic hyperplastic polyps in a domestic general population, as most symptomatic or high-risk patients can receive a colonoscopy examination free of charge under the current NHI reimbursement policy in Taiwan. To our knowledge, this is the first study that has attempted to explore the prevalence of and factors associated with both lesions simultaneously in an asymptomatic Chinese population.

Previous studies have investigated the prevalence of various types of colorectal lesions in different populations. For example, the prevalence of adenocarcinoma (including adenoma and carcinoma) at a domestic metropolitan area medical center was 15.4% [16]. In an asymptomatic population, of which 96.8% were male and the mean age (range) was 62.64 (50-75) years, the prevalence rates of advanced colorectal neoplastic polyps and hyperplastic polyps

Table 2. Comparison of clinical characteristics between neoplastic polyps and hyperplastic polyps.

Groups	Neoplastic polyps		Hyperplastic polyps		p-value
Variables	n	(%)	n	(%)	
Number					
1~2	54	(81.82%)	46	(90.20%)	0.2023
3~11	12	(18.18%)	5	(9.80%)	
Size (cm)					
0.2~0.3	22	(52.38%)	34	(80.95%)	0.0055 *
0.4~3.5	20	(47.62%)	8	(19.05%)	

*: A chi-square test p- value < 0.05.

Table 3. The results of the logistic regression analysis.†

Groups	Neoplastic polyps			Hyperplastic polyps		
Variables	OR	95%CI	p-value	OR	95%CI	p-value
Cigarette smoking, user vs. no	2.171	(1.225, 3.848)	0.0079*	1.783	(0.964, 3.296)	0.0652
Alcohol drinking, user vs. no	1.877	(1.067, 3.300)	0.0288*	--	--	--
Age (yrs)	1.034	(1.009, 1.060)	0.0069*	1.027	(1.001, 1.054)	0.0407*
BMI (Kg/m2)	1.134	(1.049, 1.226)	0.0016*	1.084	(0.995, 1.180)	0.0658
FBS (mg/dl)	1.007	(1.000, 1.013)	0.0351*	--	--	--
Cholesterol (mg/dl)	0.991	(0.984, 0.998)	0.0159*	--	--	--
Uric acid (mg/dl)	--	--	--	1.213	(1.013, 1.452)	0.0358*
Hypertriglyceridemia, yes vs. no	--	--	--	0.500	(0.235, 1.062)	0.0712
Asthma, yes vs. no	4.166	(1.014, 17.118)	0.0478*	--	--	--

*: p- value < 0.05. †: OR, odds ratio; CI, confidence interval.

were 10.5% and 12.5%, respectively [11]. In contrast, in a population of Hispanic veterans of which 99% were male with a mean age (range) of 67.5 (36-87) years, the prevalence rates of colorectal neoplastic polyps and sporadic hyperplastic polyps were 90.1% and 9.9%, respectively [13]. In a symptomatic Japanese population, the prevalence rates of both colorectal adenomas and hyperplastic polyps were 47% [17]. Those prevalence estimates were higher than the overall prevalence rates observed in our study (9.5% and 7.4%, respectively). The estimates reported by Lieberman et al. in 2003 were most similar to those of our older subjects (50-69 years) [11]. In addition, our Taiwanese self-paid colonoscopy population included mainly asymptomatic patients who might also possess better attitudes toward health; therefore, the prevalence of lesions among such a population might be lower than that among a symptomatic population or cohort from a clinical-based study (mostly comprising symptomatic or high-risk populations).

In this study, no cases with mixed polyps or with hyperplastic polyposis syndrome were reported. There are two possible explanations for this finding. First, hyperplastic polyposis syndrome itself is a rare condition. Second, such cases would have been classified into the neoplastic polyp group under current clinical pathological test practices that focus on only neoplastic polyps. To date, no domestic study has verified the association between hyperplastic polyposis syndrome and colorectal neoplastic polyps observed in European and American populations [2-5]. Further evidence is therefore required to evaluate this association in a domestic population. Moreover, the significance of identifying hyperplastic polyps when predicting colorectal tumorigenesis should be continually emphasized by clinical societies (both physicians and technologists).

Previous studies have noted that obesity-related factors such as weight, diabetes mellitus, high serum total cholesterol level, and high serum triglyceride level can affect colonic tumorigenesis [18]. Those factors might also be expected to correlate with the risk of colorectal lesions. In this study, positive associations were observed between the risks of both polyps and a high BMI level, as well as between the risk of colorectal neoplastic polyps and the fasting blood sugar level, whereas inverse relationships were observed between the risk of neoplastic polyps and the serum total cholesterol level, as well as between the risk of hyperplastic polyps and hypertriglyceridemia. The inverse relationship between the risk of neoplastic polyps and the serum total cholesterol level was also observed by Lieberman et al. in 2003 [11]. In addition, earlier studies revealed that obesity-related factors (e.g., type II diabetes mellitus, elevated BMI, and elevated serum insulin levels) were segment-specific risk factors for colon cancer and hyperplastic polyps in the proximal, but not distal, colon [17,19]. Further studies are needed to re-examine the location-dependent association between colorectal lesions and obesity-related factors.

The present study contained several limitations. First, many potential associated factors could not be determined in a retrospective study, including genetic examination outcomes, acquired factors (e.g., diets, lifestyles, and regular medications), or the frequency of common addictive substance use (e.g., cigarette, alcohol, betel nuts, and coffee). Associations between the prevalence of either type of lesion and the biochemical indexes observed in this study could also be attributed to those unmeasured potential confounders. Additional investigations regarding the associations between those factors and the risk of colorectal lesions will be required to increase our understanding of differences between populations with either type of colon lesion and those without polyps. Second, previous studies supported the viewpoint of segmental heterogeneity with respect to colorectal lesion epidemiological studies [17-20]. However, the present study did not have sufficient power to detect segment-based associations between colorectal lesions and risk factors because of the relatively small number of cases with colorectal lesions. We encountered the same limitation in our attempt to perform a lesion type-based analysis. Extended studies will be needed to evaluate the site-specific epidemiology of colorectal lesions. Finally, a self-paid health examination population might differ from the general population in various aspects of health knowledge and beliefs; accordingly, the generalizability of the current results should be considered cautiously.

Although this study reported only preliminary results, it has provided information to support future research regarding further stratification of the colorectal lesion deterioration risk in the domestic population. In particular, other researchers should consider adjusting for the effects of age, smoking, and

obesity on the risk of colorectal lesions before performing their studies. Association analyses revealed that both types of lesions were associated with known colorectal cancer risk factors (smoking, age, and BMI), and that cases with sporadic hyperplastic polyps differed significantly in only a few characteristics (e.g., FBS). Furthermore, uric acid levels differed significantly between patients with only hyperplastic polyps and controls. In conclusion, cases with sporadic hyperplastic polyps should not be considered polyp-free, although further studies are needed to clarify the differences between patients with either type of polyp.

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自費大腸鏡檢群體中的結直腸腫瘤性息肉與偶發性增生型息肉的盛行率及相關因素

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摘要

背景與目的：許多實證的更新使得增生型息肉分類及其與大腸直腸癌的相關性更為明確。現行大腸鏡篩檢策略將具有小的、少數偶發性增生型息肉且無大腸直腸腫瘤性息肉病史者視同無息肉。本研究探討腫瘤性息肉、增生型息肉、無息肉三類個案之臨床觀察的差異，及無症狀群體中偶發性增生型息肉與腫瘤性息肉的盛行率與相關因素。

方法：以回顧性橫斷面研究設計收集 755 例個案，均為來自 2009 年 1/1~9/30 間於某區域醫院的自費健檢方案下接受全大腸鏡檢查的個案。藉由病歷回溯獲得人口學、常見成癮性物質使用、生化測量值、共病症及病變組織的病理診斷資料，依診斷結果將個案分入腫瘤性息肉組、增生型息肉組、對照組。

結果：腫瘤性息肉與增生型息肉的總體盛行率分別為 9.5% 與 7.4%。這兩種病變的盛行率在男性中均較高，其個案特徵大部分無顯著差異，且都與吸煙、高齡、高 BMI 指數具相關性。校正吸煙、年齡與 BMI 後，與對照組相比，有增生型息肉的個案顯著地易有較高的尿酸值（OR =1.21，95%CI：1.01-1.45，P =0.036）。

討論：本研究探討本土族群中兩種腸道病變的流行病學特徵，資料來源為自費健檢資料庫，這類族群相當類似於無症狀群體。結果顯示：兩種病變都具有與大腸直腸癌相同的危險因素（吸煙、年齡和 BMI），且與對照組比較下有增生型息肉的個案具有不同的特徵。因此，有增生型息肉的個案不應被視同沒有息肉的個案；然而，兩類個案的差別尚有賴進一步研究釐清。

關鍵詞：大腸鏡檢、腫瘤性息肉、增生型息肉

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Case Report

A Case of Acute Nontraumatic Cervical Myelopathy Presenting as Acute Ipsilateral Hypoesthetic Hemiparesis

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Abstract

A 40-year-old man presented with sudden onset of left limb weakness and numbness upon getting up. Neurological examination revealed left hemiparesis with ipsilateral decreases in pain and touch sensation. Brain computed tomography was unremarkable. Initial impression was acute lacunar infarction, so oral antiplatelet therapy and work-up for stroke in the young were started. However, there was progression of hemiparesis. Brain magnetic resonance imaging (MRI) was unremarkable, but cervical spine MRI demonstrated intervertebral disc herniation with cord compression. Oral antiplatelet therapy was discontinued; the patient was placed on cervical orthosis, and intravenous corticosteroid was administered. Eventually, he underwent surgical decompression. The muscle strength recovered fully and the sensory defects disappeared one week after surgery. Cervical disc herniation with acute nontraumatic myelopathy may mimic acute lacunar infarction at initial presentation. Although rare, this differential diagnosis should be kept in mind considering that its management entirely differs from that of stroke.

Key words: cervical disc herniation, acute non-traumatic myelopathy, hypoesthetic hemiparesis, young stroke, dissociated hypoesthesia/anesthesia

Introduction

Cervical disc herniation is more common in men and often occurs in the age range of 22–74 years (mean, 49.7 years) [1]. Depending on the location of herniation and degree of canal compromise, the resultant myelopathy could manifest as gait disturbance, spasticity, hand numbness, chest and abdominal discomfort, position and sensory disturbances, central cord syndrome, sphincter dysfunction, or muscle atrophy [1]. In the literature, cases of acute nontraumatic myelopathy caused by cervical disc herniation most commonly presented with Brown-Sequard syndrome followed by acute paraplegia and tetraplegia [2]. Here, we report this rare case that presented with acute onset of unilateral hemiparesis and hypoesthesia without pain.

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Case Report

A 40-year-old man came to our emergency department because of inability to walk after a sudden onset of left limb weakness and numbness upon getting up in the early morning. There was no pain, vertigo, tinnitus, headache, blurred vision, double vision, dysarthria, dysphagia, aphasia, or bladder dysfunction. He used to smoke one pack of cigarettes daily for 10 years (10 pack-years), but he quit 7 years ago. He was not addicted to alcohol, areca, or any illegal drug. He has been engaged in educational management in an elementary school for

over 10 years. Four years ago, he was diagnosed with peptic ulcer disease for which he took proton-pump inhibitors for three months. He did not have hypertension, diabetic mellitus, hyperlipidemia, heart disease, or major trauma.

On physical examination, his height was 177 cm; weight, 78 kg; body mass index, 24.9 kg/m^2; body temperature, 36.8°C; blood pressure, 139/89 mmHg; heart rate, 74/min; and respiratory rate, 20/min. He was conscious and coherent, with intact cranial nerve functions. Muscle power was graded 5/5 and 5/5 (Medical Research Council Scale) in the right upper limb and lower limb, respectively, and left upper limb was graded 4+/5 and 4/5 in the left upper limb and lower limb, respectively. Pinprick and light touch sensations were decreased, whereas sensations of vibration and joint position were intact in the left-sided trunk and extremities. Deep tendon reflexes were normal on all four limbs. Bilateral Babinski plantar extensor responses were flexion; Hoffman sign was negative. Finger-to-nose and heel-knee-shin tests revealed no dysmetria. There were no involuntary movements. Brain computed tomography (CT) did not show abnormal intracranial density. On the basis of these findings, a diagnosis of sensorimotor lacunar infarct was made. The National Institute of Health Stroke Scale (NIHSS) score was three, and recombinant tissue-plasminogen activator was not given. Oral aspirin (300 mg) was administered immediately, and a stroke risk survey was conducted. The plan was to continue antiplatelet therapy during hospitalization.

On the first day in the ward, the patient experienced progressive numbness and weakness of his left limbs; muscle power was graded 4+/5 and 5/5 in the right upper limb and lower limb, respectively, and 4/5 and 3/5 in the left upper limb and lower limb, respectively. Emergency brain magnetic resonance imaging (MRI) did not demonstrate any acute infarction (Fig. 1A), but an ambiguous herniated lesion at the C4-C5 level was accidentally found on sagittal view (Fig. 1B). We then considered a potential pathology in the cervical spine as the cause of the left hemiparesis with

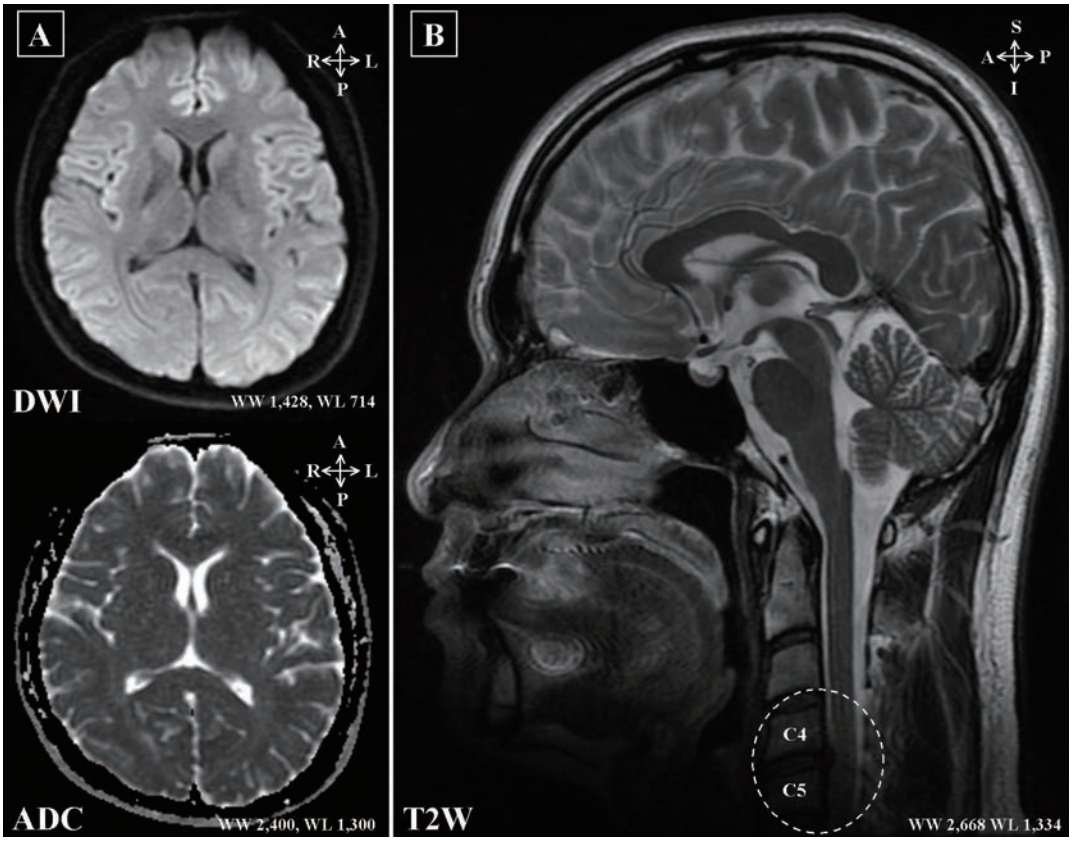

Fig. 1 (A) Diffusion weighted images (DWI) and apparent diffusion coefficient mapping (ADC)(TR/TE: 6,500/73) of the brain were unremarkable. (B) The sagittal view of brain T2-weighted imaging (T2W)(TR/TE: 3,933.34/98.12) demonstrated an ambiguous herniated lesion (dotted round circle) at the C4-C5 levels.

hypoesthesia and the new-onset right upper limb paresis. Hence, cervical spine MRI was immediately performed, which, to our surprise, revealed posterior central cervical disc herniation at the C4-C5 and C5-C6 levels; herniation was more prominent in the former and compressed the ventral surface of the spinal cord (Fig. 2). With these findings, oral aspirin was stopped and 5 mg dexamethasone phosphate was intravenously given every 8 hours. A rigid neck collar was placed for immobilization.

On the second day, muscle power on the left extremities was grade 4+/5 in the upper and 4/5 in the lower. Four days later, he underwent anterior cervical discectomy and artificial disc fusion at C4-C5 and C5-C6 (Fig. 3A). One week after surgery, muscle strength fully recovered to grade 5/5 in all four limbs and the sensory defects disappeared. The patient was discharged from the hospital. There was no recurrence of weakness or numbness during the three months of follow-up.

Discussion

Approximately 10%-14% of ischemic strokes occur in adults aged 18-45 years; among them, 51% are male [3]. Despite the fact that young adults with stroke always undergo MRI or CT for lesion topography and a wide spectrum of diagnostic tests, including extensive blood tests, Holter monitoring, and echocardiography, the etiology remains undetermined in 9% [3]. As exemplified by this case, other stroke mimickers such as cervical disc herniation with acute nontraumatic myelopathy may account for the undetermined etiology of stroke-like symptoms in the young. Therefore, this differential diagnosis of stroke should be kept in mind, especially in a young patient in whom cerebrovascular disease is not common, because the corresponding treatment will be entirely different.

Disc herniation accounts for approximately 23% of cervical myelopathy [1]. Since C4-C5 is the level with the greatest rotation and flexion–extension movement [4], it may be more vulnerable to disc herniation

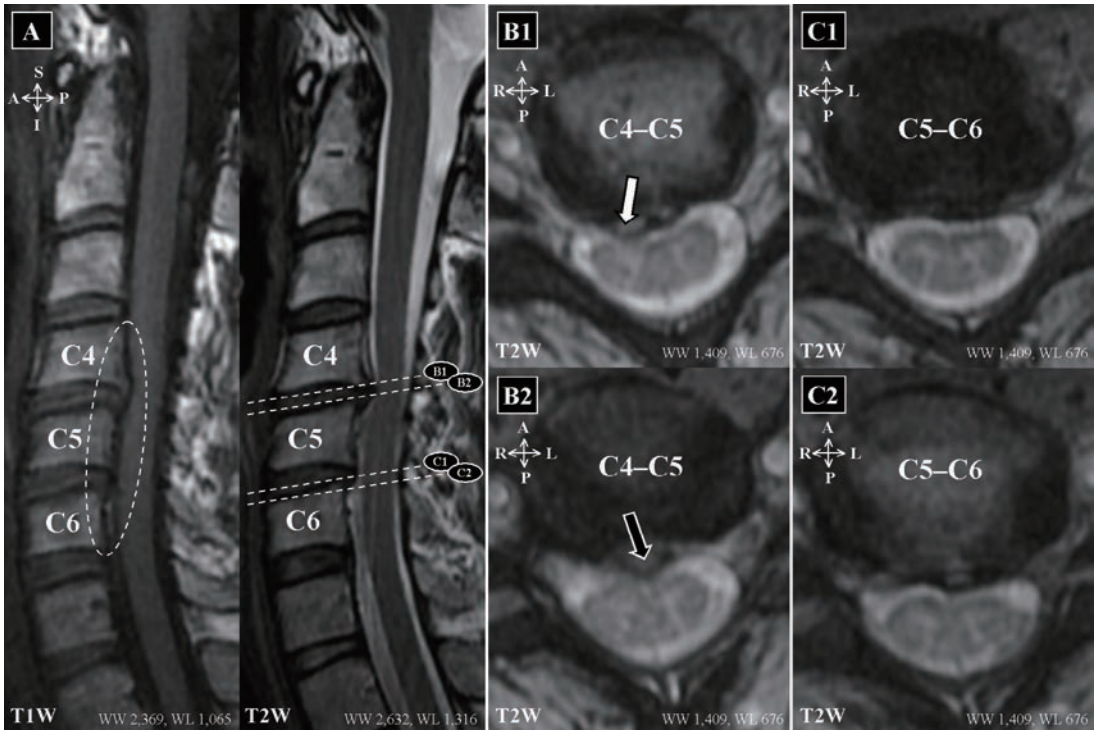

Fig. 2 (A) T1-weighted (T1W)(TR/TE: 2,116.11/37.2) and T2-weighted imaging (T2W)(TR/TE: 2,916.67/101.808) of the cervical spine demonstrated posterior central cervical disc herniation (dotted oval circle) at the C4-C5 and C5-C6 levels; herniation was more prominent in the former and compressed the ventral surface of the spinal cord. (B) the axial T2W view (TR/TE: 581.595/12.894) of dotted line B1 and B2 demonstrated the hyper-intense herniation at C4-C5 having an oblique edge; its superior part was a paramedian type and rightward-posteriorly (hollow arrow) compressed the right part of the cervical spinal cord whereas its inferior part was the median type and leftward-posteriorly (filled arrow) compressed the left part of cervical spinal cord via a midline way. (C)the axial T2W view (TR/TE: 581.595/12.894) of dotted line C1 and C2 demonstrated the hyper-intense herniation at C5-C6 did not compress the cervical spinal cord.

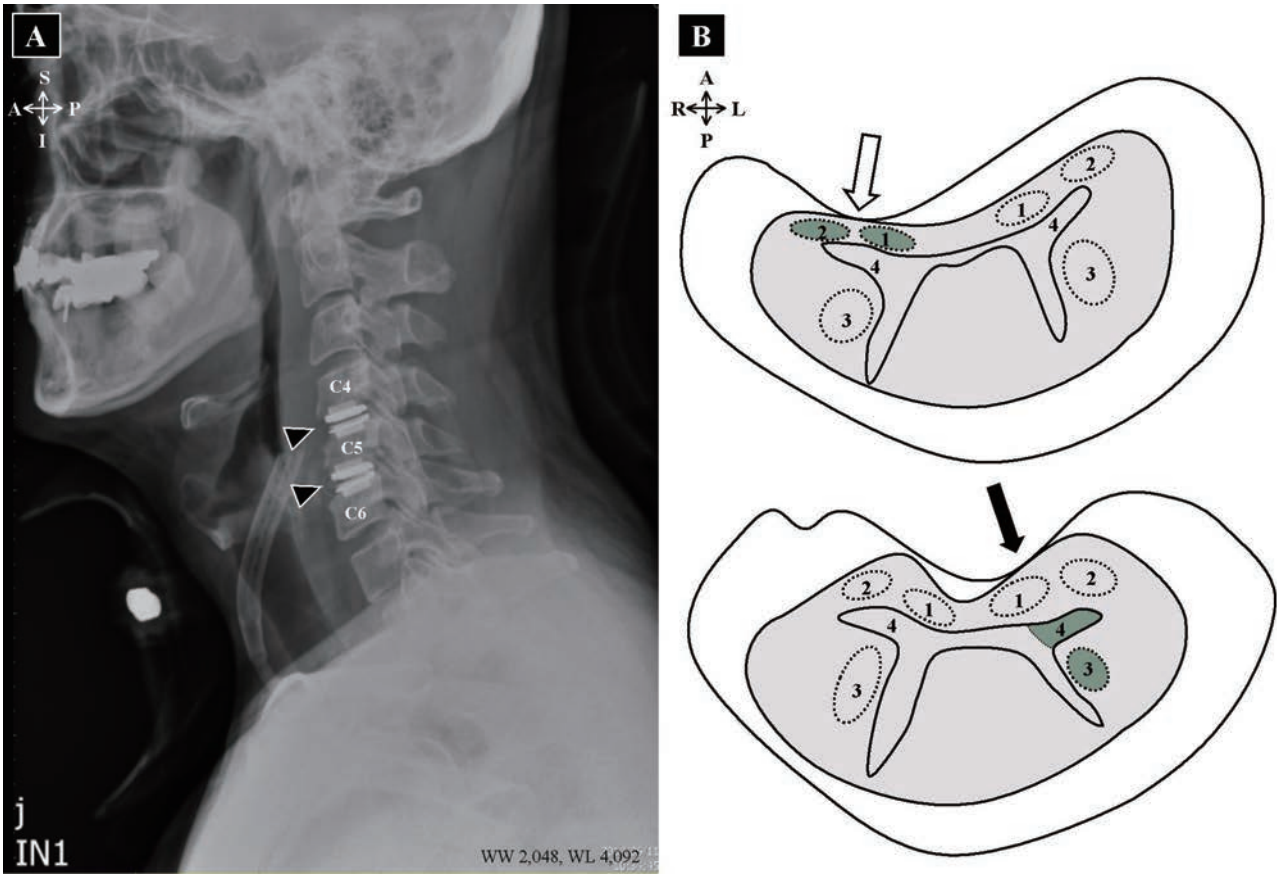

Fig. 3 (A) The post-operative lateral neck X-ray demonstrated the artificial disc insertion (arrow-heads) at C4-C5 and C5-C6. (B) In the current case, the disc herniation in C4-C5 showed an oblique edge; its superior part (hollow arrow) was the paramedian type, rightward-posteriorly compressed the right part of the cervical spinal cord, and directly affected the right anterior spinothalamic tract (tract 1, gray) and lateral spinothalamic tract (tract 2, gray); and, its inferior part (filled arrow) was the median type, leftward-posteriorly compressed the left part of cervical spinal cord via the midline, and indirectly affected the left lateral corticospinal tract (tract 3, gray) and anterior column (tract 4, gray).

in young people with minimal degenerative changes [5]. MRI, rather than CT or X-ray, provides the best radiographic evaluation of cervical disc pathology. A paramedian herniation shows more predominant clinical symptoms than the median type [1]. In the current case, the disc herniation at C4-C5 showed an oblique edge (Fig 3B). Its superior part was paramedian type with posterior compression of the right side of the cervical spinal cord; this directly affected the right spinothalamic tract, which induced the left-sided trunk and limb hypoesthesia below the C4 level. Its inferior part was median type with posterior compression of the left side of the cervical spinal cord, which indirectly affected the left lateral corticospinal tract and anterior column, inducing paresis of the left trunk and limb muscles innervated below the C4 level. Since the dorsal column was spared from compression, vibration and joint position remained intact; this, in effect, was a representation of dissociated hypoesthesia/anesthesia.

In general, cervical disc herniation responds well to nonsurgical treatment, including relative rest, cervical orthosis, analgesic medicine, traction, and physical training [6]. For patients with motor deficits, there has been no consensus on the appropriate timing of surgical intervention[1]. Symptoms presenting acutely may be related to a sudden interruption of blood flow to the spinal cord, which can induce severe ischemia and acute edema of the spinal cord. The chances for an irreversible injury are sustained as long as there is compression; hence, this kind of nontraumatic myelopathy should be detected and treated as early as possible [1]. Since our patient had acute painless neurologic deficits, acute cerebrovascular event was

highly suspected. Intravenous corticosteroid was given to address the potential edematous change until he received surgical intervention to decompress the spinal cord 5 days after symptom onset. The muscle strength recovered fully and the sensory defects disappeared one week after surgery. Thus, the importance of early diagnosis and correct treatment can never be overemphasized.

Our patient had few risk factors for stroke and as such, cervical myelopathy should be an important differential diagnosis for the acute neurologic weakness. In addition, the sensory tracts of vibration/joint position, light touch, and pain/temperature lie closely in the thalamus and cerebrum but are markedly separated in the brainstem and spinal cord; hence, the presence of dissociated hypoesthesia/anesthesia should raise the suspicion of a brainstem or spinal cord injury [7,8].

Conclusion

Although rare, cervical disc herniation with acute nontraumatic myelopathy may mimic acute lacunar infarction at initial presentation. As the corresponding treatments would be entirely different, this differential diagnosis for stroke should be kept in mind, especially in patients with few atherosclerotic risk factors and those presenting with dissociated hypoesthesia/anesthesia.

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一病例報告以急性感覺減弱性半側偏癱為表徵之急性非外傷性頸部脊髓病變

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摘要

一 40 歲男性，因急性左側肢體無力及感覺減弱急診於本院。理學檢查顯示左半側偏輕癱，該側對刺痛及輕觸等感覺減弱，腦部電腦斷層無異常發現，臆斷為急性腦小孔狀腦梗塞，故給予抗血小板劑治療，並進行年輕型中風風險因子探查。然而，住院後左側肢體癱瘓加重，腦部磁振造影無異常發現，但頸部磁振造影顯示頸部椎間盤脫出，合併頸部脊髓壓迫。遂更改治療策略為頸圈固定及靜脈注射類固醇，神外建議手術治療。頸部椎間盤脫出併發急性非外傷性脊髓病變在初期會十分類似急性小孔狀腦梗塞，縱然很少見，但仍要提高警覺，畢竟治療策略與腦中風截然不同。

關鍵詞：頸部椎間盤脫出、急性非外傷性脊髓病變、感覺減弱性半癱、年輕型腦中風、分離性感覺缺失

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Case Report

Acute Lobar Nephronia with Negative Urine Cultures Presenting with a Palpable Painful Mass: A Case Report

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Abstract

Children with severe urinary tract infections such as acute pyelonephritis and acute lobar nephronia, presenting with a fever and abdominal mass are not common. Such cases are generally mistaken as intra-abdominal abscess. Without early identification, aggressive antibiotic treatment, or even surgical drainage, acute lobar nephronia may progress to renal abscess or emphysematous pyelonephritis. Here, we report the case of a female aged 11 years and 7 months who presented with fever and a palpable mass located in the right lower quadrant. Computed tomography confirmed a diagnosis of acute lobar nephronia; however, the urine culture was negative. Treatment with intensive antibiotics (ceftriaxone and metronidazole) was adequate, and drainage was not required. With early diagnosis, such patients can be safely treated medically.

Key words: ALN; CT; 99mTc-DMSA; Palpable mass

Introduction

Acute lobar nephronia (ALN) was first described by Rosenfield et al. in 1979 as acute focal bacterial nephritis. This condition is the acute progression of a renal bacterial infection without liquefaction and typically involves one or more lobes or lobules of the kidney [1]. Without timely management, ALN may lead to acute kidney injury, renal scarring, renal or perinephric abscess, end-stage renal disease, and even death. The incidence of ALN among Taiwanese children with a febrile urinary tract infection (UTI) is 8%-10% [2].

The clinical manifestations of ALN are progressive and include lethargy, irritability, dysuria, nocturia, urinary frequency, recurrent fever, chills, and abdominal tenderness. The typical clinical triad of pyuria, bacteriuria, and flank pain varies between patients [3]. In addition to the clinical presentation, the diagnosis of UTI can be definitively determined through a positive urine culture collected from clean mid-stream urine, catheterization, or suprapubic aspiration. The threshold of diagnosis depends upon the quality of the urine specimen and the false-positive rate of the test [4]. In this study, we report a case of ALN that presented as a palpable mass without a positive urine culture.

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Case Report

A female aged 11 years and 7 months was admitted to the hospital because of intermittent fever up to 40°C that had lasted for 5 days. Her menophania occurred when she was 10-years-old. Her menses were nearly regular, without menorrhagia and menometrorrhagia. Her last menstrual period occurred 13 days before admission. She had a past medical history of allergic rhinitis, chronic sinusitis, and amblyopia.

The child was normal until 2 weeks before admission, when she developed lower abdominal pain. The pain was excruciating, with a progressive onset

that originated in the right lower quadrant without radiating to the right groin or flank. Her appetite was slightly reduced, without nausea, vomiting, hematochezia, fever, or mense. The pain was unaffected by position. She became febrile with a temperature up to 40°C 5 days before admission; she went to see a general physician on the day of fever onset. Antipyretic medication and an oral antibiotic (cephalexin) were prescribed.

Unfortunately, over the following 4 days, she continued to have intermittent fever with chills that was not relieved by prescription of diclofenac acid. She also complained of abdominal pain shifting to the right lower quadrant, accompanied by nausea and two episodes of non-bloody, non-bilious emesis. There were still no other remarkable symptoms such as dysuria, body weight loss, cough, sore throat, chest pain, diarrhea, or urinary frequency. She also reported no recent travel, exposure to new foods, or contact with sick individuals.

On physical examination, the patient appeared uncomfortable. Her vital signs were as follows: temperature, 38°C; blood pressure, 93/66 mmHg; pulse rate, 88 beats/minute; and respiratory rate, 18 breaths/minute. Her body weight was 44 kg and body height was 152 cm. Both values were between the 50th and 75th percentile. Findings on examination of the abdomen were unremarkable on visual inspection, with hypoactive bowel sounds and no bruits. The abdomen was distended, with diffuse tenderness on deep palpation of the right lower quadrant, without rebound tenderness or guarding. A firm movable mass approximately 3 cm × 3 cm was detected. There was no tenderness at the costovertebral angles on either side. Other systemic examination was essentially normal.

Notable hematologic laboratory values were as follows: leukocytosis, 15,500 (neutrophils, 84.2%; lymphocytes, 9.1%; monocytes, 6.5%; eosinophils, 0.1%; basophils, 0.1%); blood urea nitrogen (BUN), 77 mg/dL (normal, 8-25); creatinine, 3.9 mg/dL (normal, 0.6-1.5); and C-reactive protein, 38.1 mg/dL (normal, 0-0.8). Blood and urine were cultured. The urine culture obtained initially revealed no bacterial colonization. However, the urine was positive (++) for leukocyte esterase and bacteria.

Ultrasonographic (US) examination of the urinary tract (Fig. 1) showed an area of decreased echogenicity in the upper pole of the right kidney; no distal shadows were observed. Absence of the sign of the cortical rim was noted about the right kidney. A poorly-defined, regularly-margined focal mass with hypoechogenicity was observed in the lower pole of the right kidney. The left and right kidneys were similar in size. There was no echotexture heterogeneity and no loss of corticomedullary differentiation about the left kidney. The evidence of inflammation together with abnormal renal function tests presented a clinical picture consistent with acute pyelonephritis complicated by aggravated renal function.

On the third day of hospitalization, a computed tomographic (CT) study of the abdomen and pelvis (Fig. 2), performed after the intravenous administration of contrast material, showed the left kidney was 10.4 cm in length, normal in size, and with no gas bubbles or streaks in the renal parenchyma. The right kidney was 7.7 cm in the longest width and 12.6 cm in the longest length, with multiple non-enhancing, non-calcified, ill-defined border masses that did not extend beyond the kidney into the surrounding tissue; no loculated gas or perinephric fluid collection was observed.

The patient's clinical condition improved after treatment with ceftriaxone (2 g/day) and metronidazole (0.5 g/8 h) for 10 days. The CRP value decreased to 2.7 mg/dL, and the number of white blood cells dropped to <8600. under the treatment of ceftriaxone 2gram per day and metronidazole 0.5gram per eight hours, totally ten days. The patient was discharged on the 12th day of hospitalization with complete recovery. Repeated US showed the hypoechogenic

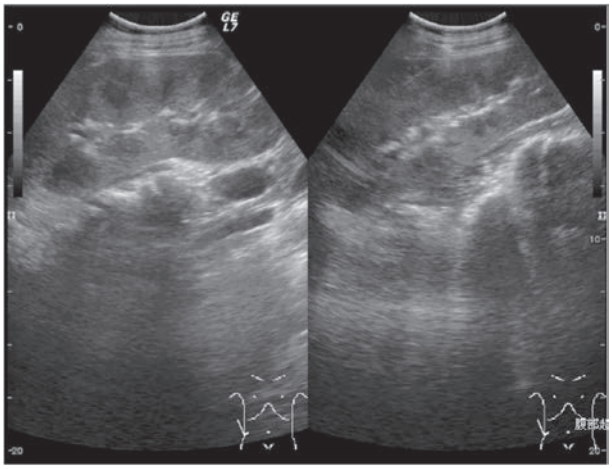

Fig. 1 Ultrasonogram of the right kidney reveals globular swelling of the right kidney with multiple hypoechoic area

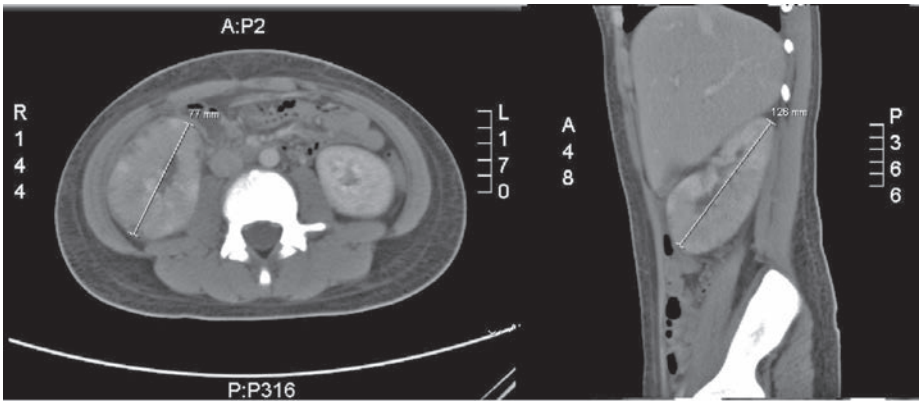

Fig. 2 A series of contrast-enhanced CT reveal the right kidney with (1) the longest width: 7.7 cm, (2) the longest length: 12.6 cm, (3) multiple low attenuated fluid collections in the subcapsular area and (4) inhomogenous nephrogram

lesion had diminished, with the right kidney exhibiting normal echotexture and volume (3.43 cm in the longest width and 11.7 cm in the longest length),contrasting that of the initial sonogram (Fig. 3). Technetium-99m dimercaptosuccinic acid scintigraphy (99mTc-DMSA) performed on the 24th day after her discharge revealed homogeneous tracer distribution in both kidneys but diffusely decreased tracer uptake in the right kidney. Scarring formation of the right kidney could not be ruled out. Diagnostic and therapeutic procedures were performed.

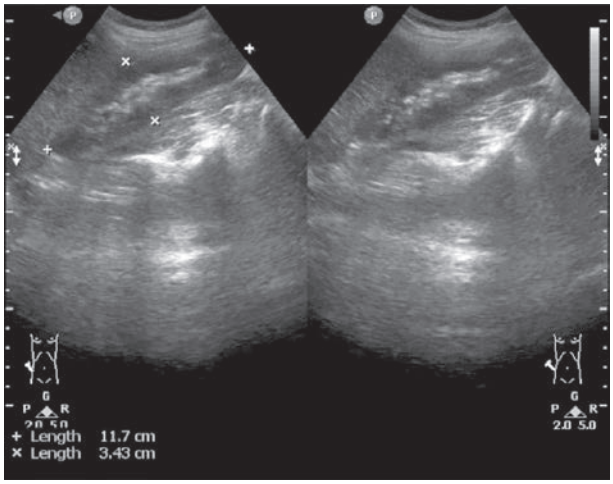

Fig. 3 Ultrasonogram of the right kidney reveals smooth surface, 3.43 cm in the longest width, and normally iso-to-slightly hypoechogenicity

Discussion

The common clinical presentation of ALN includes fever, chills, and flank pain. In this case, we observed an unusual sign of ALN, a palpable mass in the right lower quadrant. To the best of our knowledge, this is the first case of a renal mass associated with simple ALN reported in the literature. Ascending infection through ureteral reflux, by which pathogens can spread, is the most common cause of acute pyelonephritis nephronia (APN) and ALN. *Escherichia coli* is the most frequent uropathogen, causing 75%-90% of all UTIs [4]. Therefore, the diagnosis should take into account both the type of bacteria in the urine sample and the patient's symptoms. However, a dilemma may arise, similar to that with our patient, when strong clinical evidence of a severe urinary tract infection such as APN or ALN is accompanied by low bacterial counts or a negative urine culture. If the clinical findings suggest APN or ALN but the urinary culture is negative, the clinician should consider the following possible confounding factors: improper collection of the urine sample, administration of antimicrobial agents to the patient before culture, presence of urine concentration defects, and ureteral obstruction without adequate drainage via the urinary collecting system (latent abscess) [6]. In addition, UTIs with negative cultures can be caused by anaerobic bacteria (responsible for 0.8%-1.5% of UTIs), slow-growing agents such as fungi, and *Mycobacteria* in the urinary tract [7]. In the case of our patient, the negative urine culture likely resulted from diminished growth in culture because of her previous use of antibiotics. Despite the negative culture, the diagnosis of ALN was accurate based on the typical CT image.

Definitive diagnosis of ALN by radiologic imaging is based on the presence of a wedge-shaped distribution of inflammation [1]. Contrast CT is currently the

gold standard diagnostic tool for ALN, which typically appears as a poorly-defined striated or wedge-shaped lesion with decreased enhancement. In contrast to CT, US detects ALN as a central anechoic area with poorly-defined margins, with a specificity of 62%-90% and a sensitivity of 90%-95% [9, 10]. Although US can overlook the subtle changes of mild pyelonephritis and often underestimates the severity of renal involvement or perinephric extension, it still has many advantages, including wide availability, relatively low expense, and no requirement for radiation or contrast materials [8].

ALN can be considered the midpoint in the progression of a urinary tract infection from the most minor manifestations of APN to the most serious intrarenal abscess. Therefore, the risk factors for ALN in children in fact are equivalent to those of APN. Important risk factors for ALN include structural anomalies, incomplete emiction, voiding dysfunction, neurogenic bladder, immunosuppression, and prolonged or overuse of antibiotics. However, a previous study reported that up to 55% of patients with ALN have no underlying co-morbidities [3, 9]. CT is a valuable diagnostic tool for patients experiencing abdominal pain accompanied by normal urinalysis because such patients may be reluctant to undergo nephrogenic or urologic procedures in the absence of other symptoms.

APN and ALN are severe diseases that can lead to extensive renal parenchyma inflammation and damage, renal scarring with a risk of hypertension, and renal insufficiency in 10%-15% of children with UTI [6]. Therefore, 99mTc-DMSA is useful not only as an initial predictor of the range of renal scarring but also as a tracker of renal mass loss, which it can measure with sensitivity, specificity, and accuracy of 90%, 95%, and 92%, respectively [6].

Another interesting factor in this case was the palpable tender mass in the patient's right lower quadrant. According to statistical data [5], the normal kidney in a female aged 11 years and 7 months is 8.79 cm long; it is 9.0303 cm long in a female under the height of 143 cm [5]. The normal renal volume at this age is 25.2-94.4 mL. Our patient's renal volume was 284.31mL (calculated as 0.5233 × 5.6 × 7.7 × 12.6 cm). Based on both size and length, our patient had nephromegaly of the right kidney. Early awareness of this condition, the availability of imaging techniques, and proper treatment with broad-spectrum antibiotics prevented damage to the renal pelvis and parenchyma and avoided ALN progression to abscess formation, despite the scarring detected by 99mTc-DMSA.

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急性大葉型腎炎以可觸及之疼痛硬塊及陰性尿液培養為表現：病例報告

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摘要

患有嚴重尿路感染的兒童，如急性腎盂腎炎和急性大葉性腎炎，以發燒和腹部腫塊做為表現者並不常見，且通常被誤認為是腹腔內膿瘍。沒有早期發現和積極的抗生素治療，甚至是手術引流，急性大葉性腎炎可導致腎膿瘍或氣腫性腎盂腎炎。我們在這裡要報導一位十一歲又七個月大的女性，以發燒和可觸及的右下腹腫塊為表現，經電腦斷層證實為急性大葉性腎炎，但尿液培養結果為陰性。她被使用適當和密集的 Ceftriaxone 和 Metronidazole 治療，最終並無放置引流管引流。憑藉早期診斷，這患者可以安全地使用藥物治療。

關鍵詞：急性大葉性腎炎、電腦斷層 、鎝 -99m 二巰基丁酸閃爍攝影、可觸及腫塊

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Case Report

Cytomegalovirus Reactivation in Acute Myocardial Infarction: A case report

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Abstract

Coronary artery disease (CAD) is associated with bacterial and viral infections. Cytomegalovirus (CMV) causes atherosclerosis and acute myocardial infarction directly and/or indirectly. Here we report the case of a 55-year-old male who was admitted to our emergency department because of an out-of-hospital cardiac arrest. The patient was rescued using cardiopulmonary resuscitation. After percutaneous coronary intervention and stenting, the coronary artery regained a Thrombolysis in Myocardial Infarction 3 flow. Full consciousness was regained on day 26. Intermittent low-grade fever was recorded after his admission, and septicemia due to bacterial infection occurring on day 6 was treated with ceftazidime, which induced an allergic reaction that was treated with steroids for 3 weeks. A severe episode of bloody stool on day 42 was stopped by local injection of epinephrine. CMV colitis was pathologically diagnosed from the biopsy. The patient was treated with valganciclovir (450 mg, q2d) for 1 month, and CMV viremia eventually resolved. Because CMV infection is more frequently associated with immunocompromised patients, this case warrants review.

Key words: Acute myocardial infarction, Cytomegalovirus

Introduction

Active cytomegalovirus (CMV) infection occurs more frequently in patients with coronary artery disease (CAD) than in healthy controls[1]. CAD is the most common cause of sudden cardiac death in adults aged over 30 years [2]. The diagnosis of acute myocardial infarction (AMI) is determined by a high clinical suspicion from the patient's history, physical examination, changes in cardiac biomarkers [creatinine kinase MB (CK-MB), troponins, and myoglobin], and electrocardiography (ECG) findings. Here we report the case of a 55-year-old male patient with an out-of-hospital cardiac arrest (OHCA) who was rescued by cardiopulmonary resuscitation followed by percutaneous coronary intervention and stenting. He regained full consciousness on day 26 thereafter. He suffered an episode of bloody stool on day 42 that was stopped with a local injection of epinephrine. CMV colitis was confirmed by pathological findings acquired using sigmoidoscopy.

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Case Report

A 55-year-old male, 170 cm in height and weighing 72 kg, felt sudden chest pain at 9 a.m. on March 25, 2014. He visited a local clinic; there he lost consciousness and collapsed because of OHCA; he was transported to our emergency medical department within 10 min by emergency medical technicians. Cardiopulmonary resuscitation (CPR) was performed immediately upon his arrival. Ventricular fibrillation was corrected using a defibrillator multiple times, continued CPR, and drugs (Fig. 1A). ECG detected a heartbeat 1 h later [52 beats per minute (bpm), junctional bradycardia] (Fig. 1B), and his blood

pressure (BP) increased from 0/0 to 73/58 mmHg. The patient's consciousness was E1VeM1 on Glasgow Coma Scale (GCS). The 12 leads ECG revealed an ST-T depression in leads V1 to V3 (Fig. 1C). AMI was highly suspected, although the initial blood test values were within normal ranges (troponin-I < 0.06 ng/mL; CK-MB = 6.4 IU/L; CK = 174U/L). Therefore, coronary angiography was performed with the consent of the patient's family. Occlusion of the left circumflex coronary artery was observed (Fig. 2), and subsequent balloon angioplasty and stenting achieved a Thrombolysis in Myocardial Infarction 3 flow. The diagnosis was AMI, Killip IV, complicated by cardiac arrest. The highest level of troponin-I was 1764.94 ng/mL.

This patient had no history of heart disease, hyperlipidemia, diabetes, or obesity (BMI = 24.9 kg/m^2). His employment was not stressful, but he was carrier for hepatitis B virus. He had a history of high BP and was a heavy cigarette smoker (2-3 packs/day) for 30 years. After angioplasty and stenting, the left ventricular ejection fraction was calculated as 43% using echocardiography, and his BP increased to 145/65 mmHg. The patient's consciousness was E1VeM3 on GCS, and his pupil size was 4 mm/4 mm, L/R: −/− (pupillary light reflex absent). He was agitated and comatose intermittently from day 2 until day 26. His

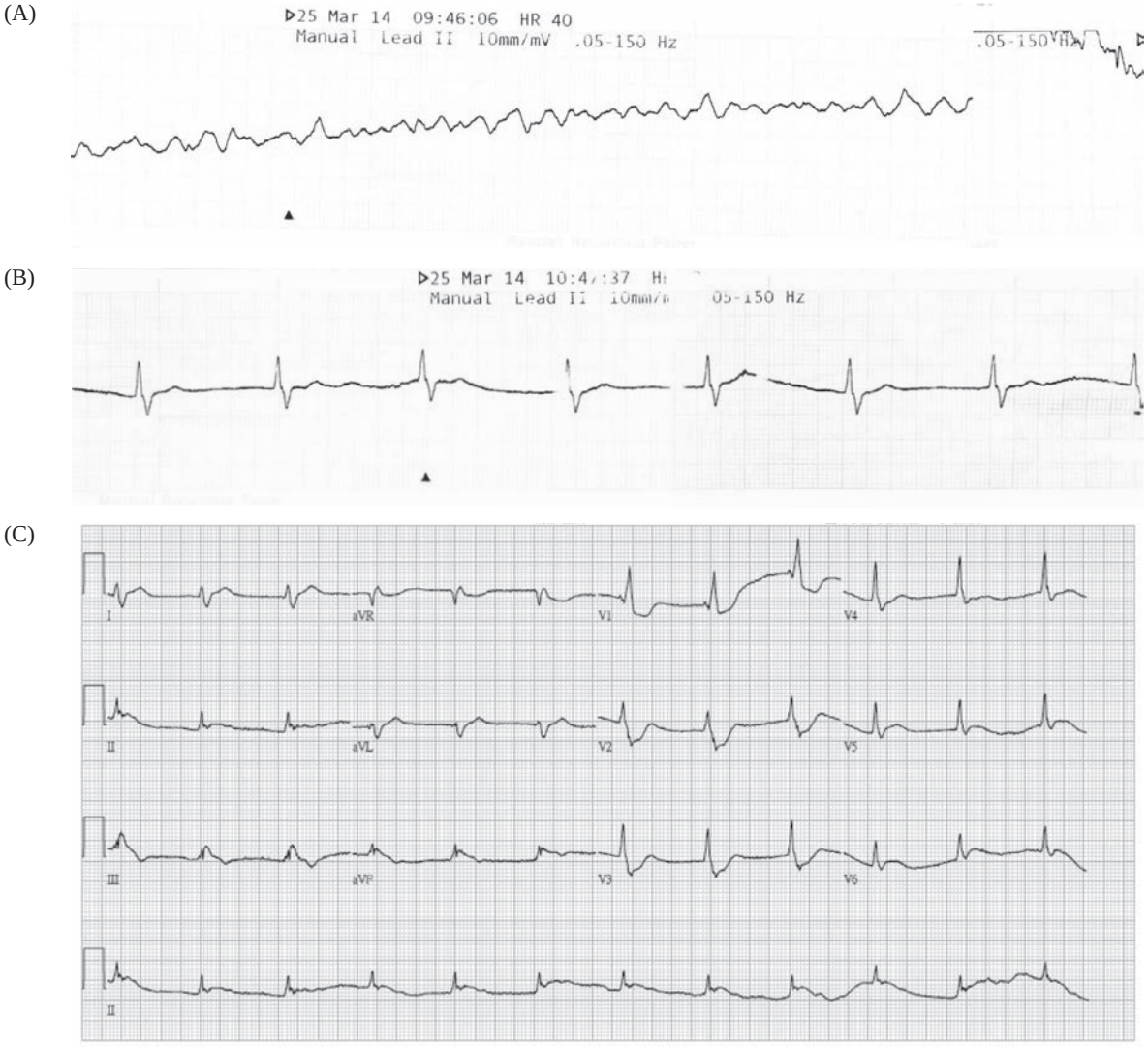

Fig. 1 Cardiopulmonary resuscitation was performed on the patient within 10 min post-cardiac arrest. Ventrical fibrillation from patient's ECG (A) was stop by several defibrillation, continuing CPR and drug treatment. Junctional bradycardia (B) with 52 bpm was developed one hour later. He had a blood pressure of 73/58 mmHg but was unconscious (GCS: E1VeM1) (C) A change of ST-T depression in leads V1 to V3 of 12 leads electrocardiogram.

eyes opened on day 4, and partial movement of his limbs was observed on day 5. The endotracheal tube was removed on day 13; however, an intermittent fever of 38°C-39°C was noticed after hospitalization.

The patient received hemodialysis three times a week from March 27 (day 2) to May 15 (day 52) to treat acute renal failure. Upper gastrointestinal (GI) bleeding on day 18 was stopped using a proton pump inhibitor. Septicemia due to bacterial infection on day 6 and Fortum (ceftazidime pentahydrate) 2 gm qd was administered starting on day 13 because of *Burkholderia cepacia* bacteremia. Methylprednisolone was used to treat severe allergy (itching and reddish edematous wheals over the trunk and limbs on day 20) caused by ceftazidime. Solu-Medrol (20 mg) was injected q12h, followed by decremental doses for 5 days, and then Metisone (2 mg, tid) was administered at subsequent decremental doses for 24 days.

However, severe bloody diarrhea (150-200 ml) occurred on day 42. Gastric endoscopic findings

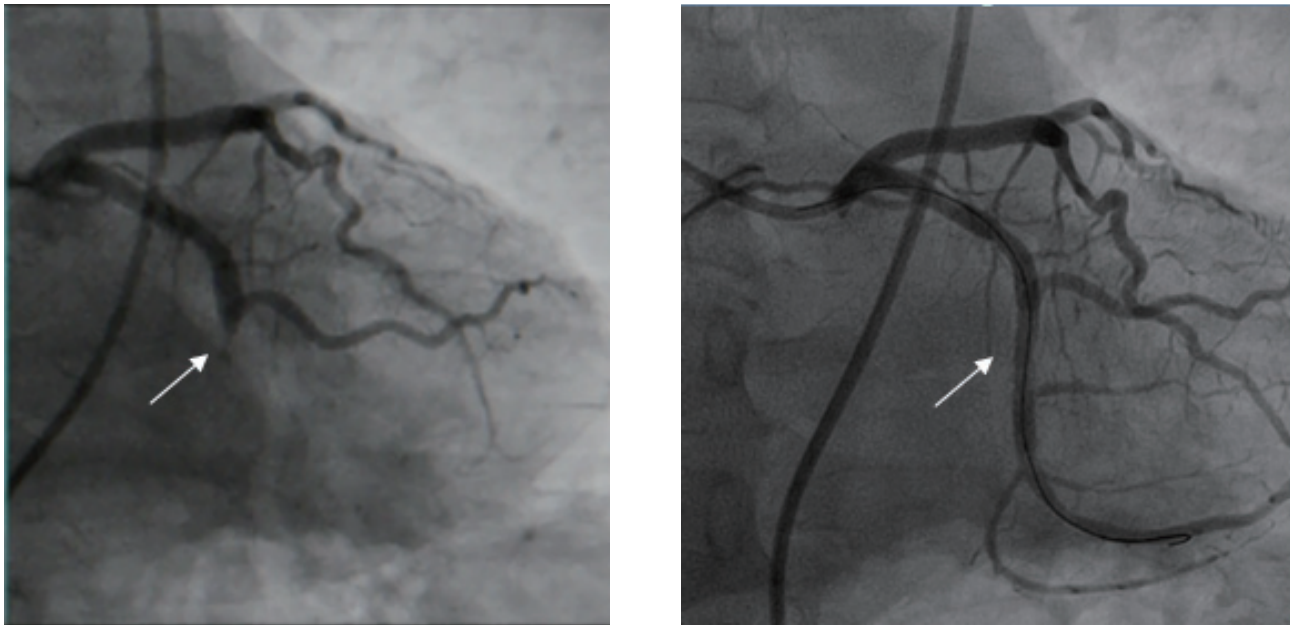

Fig. 2 Occlusion of the left circumflex coronary artery (A). Recanalization of occluded left circumflex coronary artery after angioplasty and stenting (B).

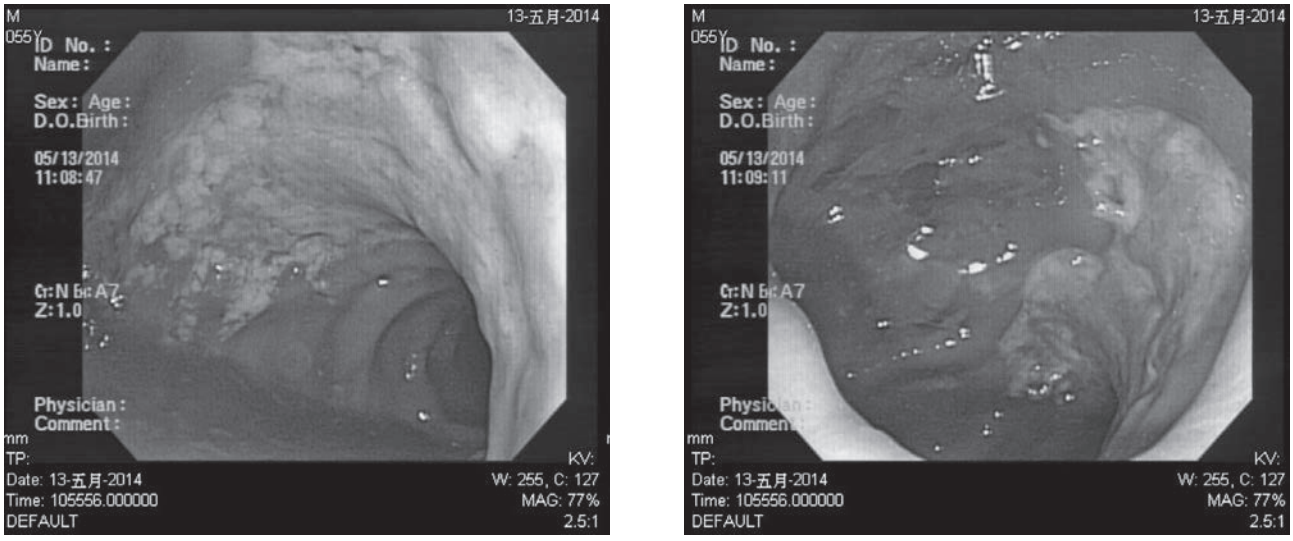

Fig. 3 Large rectal ulcer with stigmata of recent hemorrhage (SRH).

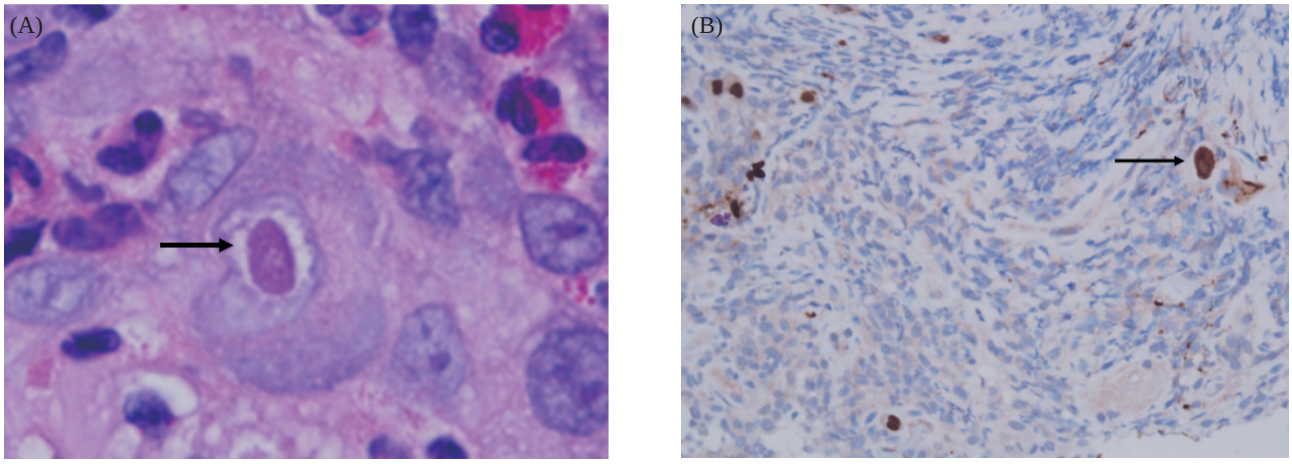

Fig. 4 A cell displays a large eosinophilic inclusion and surrounded by a clear halo with the characteristic owl's eye appearance (arrow) by hematoxylin-eosin stain (A). Numerous smaller cytoplasmic inclusions are also found (H & E stain x 1000). (B) The immunohistochemical stain shows multiple cytomegalovirus-positive cells (arrow) (IHC stain, × 200).

revealed a gastric ulcer A2 in the angularis and reflex esophagitis of Los Angeles grade A. These finding could not explain the degree of GI bleeding and unstable vital signs (BP, 87/63 mmHg, heart rate, 130 bpm). Eventually, a large rectal ulcer with stigmata of recent hemorrhage was observed using sigmoidoscopy (Fig. 3). Bloody stools stopped immediately after local injection of epinephrine. Pathological examinations showed severe colitis with ulcer formation mixed with some large atypical cells with a prominent eosinophilic inclusion body in the vascular endothelium and $CK^{-}CD20^{-}CD34^{+}CMV^{+}$ macrophages. These findings established the diagnosis of CMV colitis (Fig. 4). The highest serum CMV antibody titer was 16154 IU/ml. The patient was administered oral valganciclovir (Valcyte, 450 mg) q2d based on his insufficient renal function. Because CMV infection is common in immunocompromised patients, we tested for human immunodeficiency virus (HIV) with the patient's consent. HIV was not detected and 1 month after drug treatment, CMV was undetectable.

Discussion

Risk factors for CAD include age, sex, family history, smoking, high BP, high blood cholesterol, diabetes, obesity, physical inactivity, and high stress. This patient had a history of high BP and heavy cigarette smoking (2-3 packs/day) for 30 years. These factors may have contributed to AMI. An episode of severe CMV colitis occurred on day 42, and it was not clear whether the CMV infection caused AMI or whether CMV infection was reactivated after steroid treatment.

CMV is a double-stranded DNA virus that belongs to the Herpesviridae family (human herpes virus-5). Infection with this virus is common in humans, with seroprevalence rates ranging 40%-100% in the United States[3]. In immunocompromised patients, CMV causes life-threatening conditions including pneumonitis, hepatitis, retinitis, colitis, or encephalitis[4]. However, in immunocompetent patients, the clinical presentation of CMV infection may differ. The association between CMV infection and atherosclerosis is the subject of controversy[5,6]. For example, some studies demonstrate an association between prior CMV infection and CAD[7,8] in contrast to others[9,10]. Furthermore, CMV seropositivity indicates mainly previous exposure and does not discriminate between a latent or active infection[2]. CMV infection is characterized by alternating periods of latency and reactivation. Reactivation of CMV occurs frequently in immunosuppressed individuals such as those with transplants, HIV infection, and chronic inflammatory diseases undergoing immunosuppressants therapy[11-12]. In contrast, CMV infection in immunocompetent patients is benign and self-limited[13]. Although CMV can remain latent for an individual's entire life, CMV reactivation may result in CMV-induced end-stage organ disease in immunocompromised patients[13,14]; severe clinical manifestations of CMV infection occur in critically ill immunocompetent patients[15,16]. Moreover, there is a strong association between CMV reactivation, prolonged

hospitalization, and death[15]. The in-hospital mortality rate is reportedly 71.4% despite specific treatment with ganciclovir[16]. Lower GI bleeding in these patients is a clinical manifestation of CMV colitis and hence the provided healthcare should be alerted with regard to this condition[16].

It is possible that patients with CAD are more susceptible to CMV because of macrophage activation, endothelial cell injury, and lipid retention in atherosclerotic plaques[1,17,18]. We did not suspect a role for CMV infection in our patient with recurrent fever, until he experienced severe bloody diarrhea, which led to the pathological confirmation of CMV infection. Therefore, for patients with CAD accompanied by fever, testing for CMV, *Helicobacter pylori,* and *Chlamydia pneumonia* should be considered along with routine bacterial cultures for urinary tract and lung infections[6]. Here latent CMV infection was reactivated after 29 days of methylprednisolone treatment for antibiotic-induced allergy. A previous report indicates that latent CMV infection is reactivated after low-dose (120 mg daily) methylprednisolone treatment for 5 weeks[19]. Therefore, our findings suggest the possibility of viral involvement in atheroma during angioplasty in the presence of low-grade fever, and physicians should be made aware of the possibility of CMV reactivation induced by immunosuppressants during treatment of patients with CAD .

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急性心肌梗塞病患之細胞巨大型病毒再活化感染病例報告

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摘要

冠狀動脈疾病可能和一些特定的細菌及病毒感有關，尤其是巨細胞病毒（CMV），它能直接或間接的造成粥狀血管硬化症導致急性心肌梗塞。病例報告 : 一位 55 歲男性，因心臟停止跳動而送至本院急診室，經急救後及緊急心導管檢查，發現冠狀動脈梗塞，經氣球擴張術及支架置放後，血管恢復正常的 TIMI 3 流動。病患住院第 26 天時，才完全清醒。但住院 42 天時因嚴重血便，經乙狀結腸鏡檢發現結腸潰瘍，以 Epinephrine 局部注射處理後血便即停止。病理切片鑑定為巨細胞病毒結腸炎，給予病患口服 Valganciclovir（Valcyte 450 毫克）q2d，一個月後病毒完全清除。由於免疫功能不全病人比非免疫功能不全病人容易引起巨細胞病毒再活化感染，所以我們對此巨細胞病毒感染的成因，做文獻回顧與探討。

關鍵詞：急性心肌梗塞，巨細胞病毒

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Case Report

Complete Hydatidiform Mole: A case report

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Abstract

A 15-year-old single primigravida was transferred to our hospital for medical management of a presumed molar pregnancy. She presented intermittent uterine bleeding starting early in the first trimester. Her serum human chorionic gonadotropin (hCG) concentration was 91,816 mIU/ml and reached 1,407,359 mIU/ml upon admission. Transvaginal ultrasound revealed an enlarged uterus with "swiss cheese" endometrium, hyperechoic cystic elements, and absence of the embryo in the uterine cavity.

Suction curettage was performed for molar pregnancy. No prophylactic adjuvant chemotherapy was prescribed and no postoperative complication was encountered. The histopathological report indicated features of complete hydatidiform mole (CHM). The patient's hCG value decreased steadily postoperatively and reached the normal range within 30 days. Seventeen months postoperatively, she delivered a healthy full-term female infant.

Gestational trophoblastic disease should be considered in the differential diagnosis of young pregnant women that present with such symptoms. Early detection and treatment of CHM improve the clinical outcome.

Key words: Complete hydatidiform mole, human chorionic gonadotropin, teenage pregnancy

Introduction

A molar pregnancy is a gestational trophoblastic disease (GTD) that grows into a mass in the uterus and is characterized by swollen chorionic villi. These villi grow in clusters that resemble grapes[1]. A molar pregnancy can develop when the fertilized egg does not contain an original maternal nucleus and it may or may not contain fetal tissue[2]. However, the pathogenesis of GTD is directly associated with the fetal, not maternal tissue[1].

Molar pregnancies are categorized as partial moles or complete moles. This categorization refers to a clump of growing tissue or a growth. A complete mole is caused by a single (incidence is approximately 90%) or two (incidence is approximately 10%) sperms combining with an egg that has lost its DNA. The sperm cell then reduplicates forming a "complete" 46 chromosome set[3]. The genotype is typically 46,XX (diploid) owing to the subsequent mitosis of the fertilizing sperm. It can also be 46,XY (diploid), but 46,YY (diploid) does not occur[4]. In contrast, a partial mole occurs when an egg is fertilized by one or two sperms. The sperm cell then reduplicates itself, yielding 69,XXY (triploid) or 92,XXXY (tetraploid) genotypes[3]. Complete hydatidiform moles (CHM) have a higher risk of progression to choriocarcinoma, a malignant trophoblastic tumor, than do partial moles.

More than 80% of hydatidiform moles are benign[5]. The treatment is usually successful, but close follow-up is very important. In 10 to 15% of cases, hydatidiform moles may develop into invasive moles. This condition is known as persistent trophoblastic disease (PTD). The moles may invade so deeply into the uterine wall that hemorrhage or other complications may develop. Therefore, a full postoperative radiographic evaluation of the abdomen and chest will often be requested. In addition, patients are recommended to practice effective contraception to

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avoid pregnancy for at least 6 to 12 months[5].

In 2 to 3% of the cases, hydatidiform moles may develop into choriocarcinoma, which is a malignant, rapidly growing cancer that spreads quickly to neighboring organs. Despite these factors normally indicating a poor prognosis, the rate of cure after chemotherapy is high. Over 90% of women with malignant, non-spreading choriocarcinoma survive and retain their ability to conceive and bear children. In those with metastatic (spreading) cancer, remission remains at 75-85%, although their childbearing ability is usually lost. CHM is associated with many complications such as severe vaginal bleeding, formation of theca lutein cysts, early development of preeclampsia, hyperthyroidism, and malignant transformation[6].

CHM is currently considered a rare disease in Japan, with a decline of the estimated incidence from 1.09 in 1991 to 0.49 in 2000 per 1000 births [7]. The incidence of hydatidiform mole is 0.82-2.0 in China, 0.6-1.1 in Europe and North America, and up to 2.0 in Japan per 1000 pregnancies[8]. A study in Ireland, where all products of conception from first- and second-trimester abortions were referred for pathological examination, found that the incidence of CHM was 1:1,945 pregnancies[9]. Taken together, the worldwide incidence of CHM is approximately 0.6-2.3 per 1000 pregnancies, and it is high in the Far East, particularly in Korea and Japan. The incidence of CHM is 0.5 in 1000 pregnancies and 0.8 in 1000 deliveries[10].

Case Report

A 15-year-old single Taiwanese woman, gravida 1, para 0, reported intermittent slight vaginal bleeding starting early in the first trimester that was not associated with cramping. She initially visited to Beigang Hospital of China Medical University, ChiaYi, Taiwan. Her pregnancy was confirmed by a urine pregnancy test and an ultrasonographic examination at 5 weeks and 2 days after her last menstrual period. She then visited a local clinic in Taichung complaining of recurrent vaginal spotting, described as mild in intensity and dark in color. Her serum human chorionic gonadotropin (hCG) level was 91,816 mIU/ml. After the diagnosis of a presumed molar gestation, the patient was transferred to our hospital for further management. Upon admission, her serum hCG level was 1,407,359 mIU/mL, the hemoglobin concentration was 13.5 g/dl, and hematocrit, 39.5%. Her blood group was A, Rh-positive and her partner's blood group was O. Other biochemical parameters were within normal limits.

Apart from being slightly pale and having a short stature, she appeared quite normal on general examination. Her body weight was 39 kg and height, 145 cm. Her pulse, blood pressure, body temperature, and respiratory rate were within normal limits. There was no exophthalmos and her extraocular movements were normal. The thyroid gland was palpable and of normal size. Cardiovascular and respiratory examinations were normal. The chest radiograph was normal.

On gynecologic examination, the uterus was the size of a fist, soft in consistency without tenderness or pain with cervical lifting. Bilateral adnexal masses were impalpable. Transvaginal ultrasonographic examination revealed an enlarged uterus with "swiss cheese" endometrium, the so called "snowstorm"

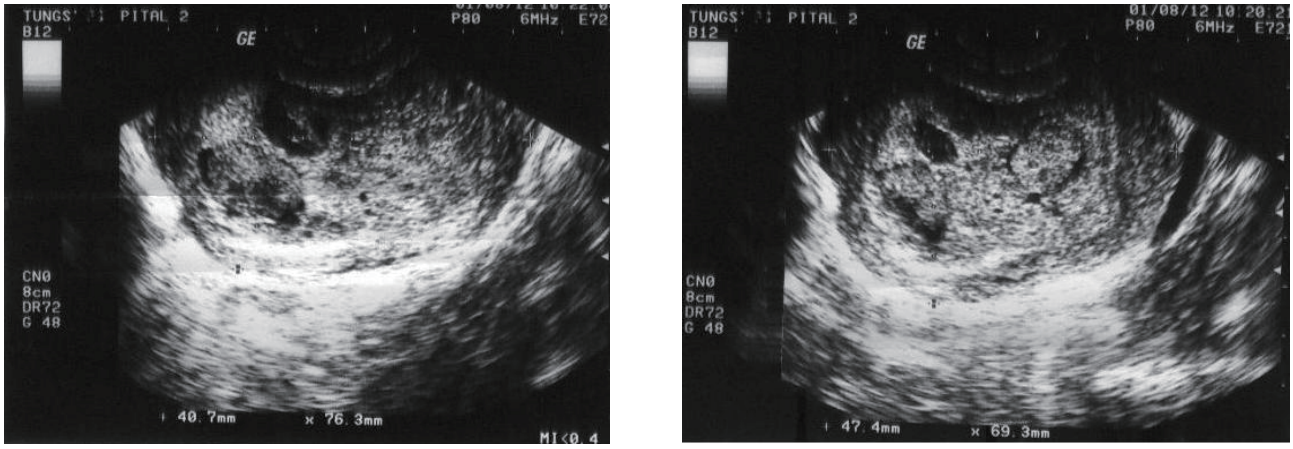

Fig. 1 Transvaginal ultrasound shows an enlarged uterus with "swiss cheese" endometrium, hyperechoic cystic elements, in the uterine cavity without embryo.

appearance, and the absence of an embryo within the uterine cavity (Figure 1). The intrauterine complex mass was 76.3 × 40.7 × 47.4 mm in size. Multiseptated ovarian cysts (ovarian theca lutein cysts) were not detected. Both ovaries were normal in size. There was no evident abdominal fluid accumulation in the Douglas pouch.

Suction curettage was performed for molar pregnancy on August 1, 2012. No prophylactic adjuvant chemotherapy was prescribed, and there were no postoperative complications. Effective contraceptive measures were advised to be implemented and maintained throughout the period of hCG surveillance. The patient's specimen consisted of multiple small pieces of endometrial tissue fragments. Microscopically, the sections showed the following findings: 1) hydatidiform mole with hydropic changes, but the villi were devoid of vessels (avascularization); 2) mild to moderate degree of trophoblastic hyperplasia. Mild trophoblast atypia with mildly increased nucleus-to-cytoplasm ratio and mild hyperplasia were also noted; 3) absence of embryo or fetal tissue (Figure 2). Moderately elevated beta-hCG (129,463 mIU/ml) on the 1st postoperative day. According to the above pathological findings, it was likely that the accurate diagnosis was CHM.

The patient's serum hCG titers decreased steadily and reached the normal range postoperatively. Postoperative hCG levels were 5.97 (Aug 9), 11.6 (Aug 21), and 3.80 mIU/ml (Aug 30, 2012), respectively. The hCG normalization time was 30 days.

She was discharged on August 2, 2012 so that she could continue with her wedding preparations. Thereafter, she was re-admitted to our ward because of a 35-week pregnancy, possible onset of premature labor, and urinary tract infection. Her thyroid function was normal (T3, 1.05 ng/ml; T4, 9.7 μg/dl; and TSH, 0.71 μU/ml). The fetal development was within normal limits at that time. Subsequently, she delivered a healthy full-term female infant, with birth

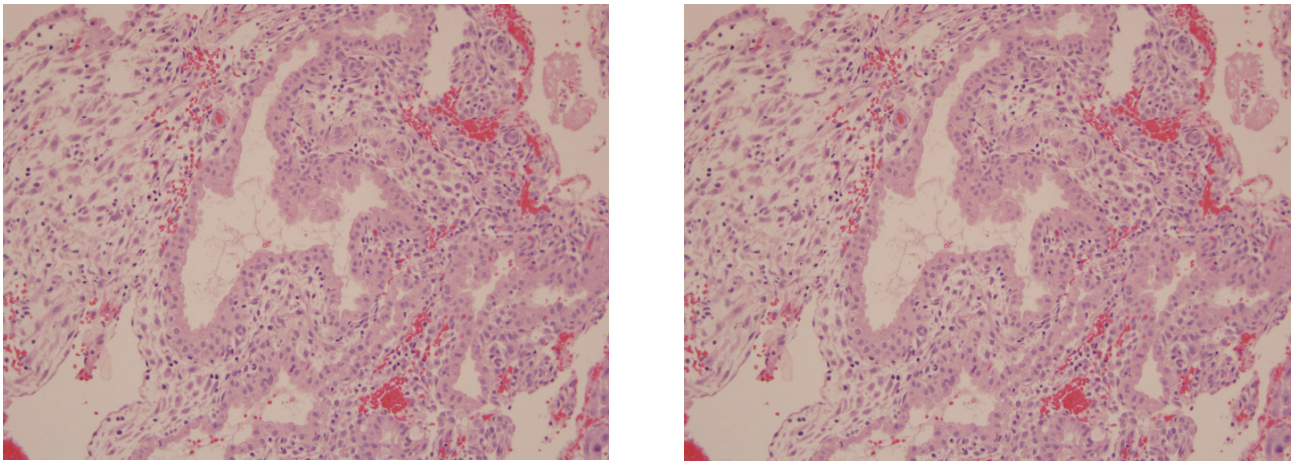

Fig. 2 Microscopic examination of hydatidiform mole. Mild to moderate degree of trophoblastic hyperplasia with hydropic changes and devoid of vessels of villi were observed.

Table 1. Modified WHO Prognostic Scoring System for hydatidiform moles

	0	1	2	4
Age	<40	≥40	–	–
Antecedent pregnancy	mole	abortion	term	–
Interval months from index pregnancy	<4	4–6	7–12	>12
Pretreatment serum hCG (IU/L)	$<10^3$	10^3–10^4	10^4–10^5	$>10^5$
Largest tumor size (including uterus)	<3	3–4 cm	≥5 cm	–
Site of metastases	lung	spleen, kidney	gastrointestinal	liver, brain
Number of metastases	–	1–4	5–8	>8
Previous failed chemotherapy	–	–	single drug	≥2 drugs

Ref [20]: Women with a score of 7 or greater are considered at high risk.

weight of 3,050 gm and normal general appearance, at the Yushen Clinic, Feng Yuan.

Discussion

CHM is a localized and non-invasive proliferative GTD with varying incidences reported worldwide[11,12]. Variations in the incidence of CHM pregnancy may partially result from differences between hospital-based versus population-based data. In South Korea, the hospital-based incidence of GTD decreased from 40.2 per 1,000 deliveries between 1971 and 1975 to 2.3 per 1,000 deliveries between 1991 and 1995[13].

The occurrence of CHM is closely related to the maternal age and previous history [14,15]. Our patient was a primigravida, without previous history of CHM. The risk of CHM is increased significantly in extremes of maternal age (i.e., < 20 and > 35 years)[14], in nulliparous women, and women whose diet is deficient in protein, folic acid, and carotene[16]. The high incidence of complete molar pregnancy in some populations has been attributed to nutrition and social economic factors[16]. Our patient was a teenager, primigravida, with a short stature. Thus, it is possible that she had nutritional deficiencies.

A retrospective study of 64 cases of molar pregnancies in Nepal show that there were 37 complete moles and 23 partial moles between 2008 and 2010[17]. The onset of the majority (67%) of cases presented early during the second trimester. Twenty one (32%) women had A positive blood group and Rh and 10 (15.6%) presented with severe anemia. The study provides detailed data regarding the incidence of partial and complete molar pregnancies with increasing maternal age. It confirms the relationship between molar pregnancy, age, and blood group. The highest incidence of gestational trophoblastic disorder was for CHM, affecting mostly younger women, and usually in the first half of the pregnancy[17]. Only two partial molar pregnancies were found among 15 cases of molar pregnancies in Tungs' Hospital between 2004 and 2014. The remaining cases were identified with gestational products, and the patient age ranged from 20 to 40 years.

Women with blood group A impregnated by men with blood group O have an almost 10-fold greater risk of subsequently developing gestational trophoblastic neoplasia than women with blood group A impregnated by partners with the same blood group. Furthermore, women with group AB tend to have a relatively worse prognosis[16]. Unfortunately, our patient had blood group A and her partner had blood group O. Therefore, this case was highly suggestive of the association of CHM and the blood group.

Because of the widespread use of ultrasonography and serum hCG test, patients with hydatidiform mole are diagnosed earlier during the gestation and the clinical features at the time of diagnosis are different from those described at later disease stages[18]. However, vaginal bleeding remains the most common presenting symptom. A study showed that vaginal bleeding occurred in 94 of 113 cases (83.2%)[19]. Of 113 cases, 52 (46%) presented excessive uterine size that lacked correspondence with the weeks of gestation. Preeclampsia, hyperemesis, hemoptysis, and theca lutein cysts occurred in 4 of 113 (3.5%), 12 of 113 (10.6%), 4 of 113 (3.5%), and 19 of 113 cases (16.8%), respectively. The incidence of postmolar gestational trophoblastic neoplasia (PGTN) was 21% (24 of 113). Comparing with historical data, the incidence of vaginal bleeding and preeclampsia was statistically lower ($p < 0.005$)[19]. The incidence of PGTN increased moderately without statistical significance compared with historical data. Therefore, the changes in patterns of clinical manifestations warrant changes in the pattern of medical practices as well. Management of molar pregnancies includes immediate surgical removal of the gestational tissue and postoperative surveillance of hCG titers. All patients with CHM should have a close serial β-hCG follow-up postoperatively because of the possibility of developing a persistent tumor. β-hCG titers should be measured every 1 to 2 weeks until they normalize. Next, they should be measured at monthly intervals for an additional 6 months[18].

Suction curettage under general anesthesia is the method of choice once the patient is deemed stable. This can be safely accomplished even when the uterus is the size of a 28-week gestation. Blood loss is usually moderate. After the completion of the evacuation, all Rh-negative patients should receive Rh immunoglobulin. Current recommendations restrict hysterotomy to cases complicated by hemorrhage. Hysterectomy remains an option for good surgical candidates who are not desirous of future pregnancy and for older women, who are more likely to develop malignant sequelae[16].

Most of the reported cases were treated primarily

with suction curettage without any associated complications[16]. This may be attributable to early intervention, which is mostly preceded by early detection of a non-viable pregnancy as estimated by the Modified WHO Prognostic Scoring System[20]. None of the cases received prophylactic chemotherapy after the primary treatment. In the present case, the patient did not receive prophylactic chemotherapy either.

The hCG median normalization period (NT) after treatment is approximately 60 days[21,22]. In our case, hCG NT was 30 days, which was similar to the data reported previously. β-hCG NT was not associated with the initial β-hCG levels and the duration of the gestation at onset. In addition, patient age, gravidity, parity, smoking, initial β-hCG levels, and ultrasonographic mean lesion size did not predict adjuvant chemotherapy requirement and did not change the type of treatment given[12].

Wolfberg et al reported that of women whose hCG level fell below 5 mIU/mL, none developed persistent trophoblastic disease[23]. Based on these findings, it might be possible to discontinue surveillance once a negative hCG value has been obtained. Nevertheless, patients are advised to avoid conception for one year after a molar pregnancy, because of the risk of having another molar pregnancy, which is approximately 0.2%[24].

Conclusions

Clinicians must be aware that, even though gestational CHM is rare, it can occur in gestating women, especially in the presence of uterine bleeding or an overly large uterus that does not correspond with the gestational age during the first or second trimester. Therefore, there should be a high level of suspicion and GTD should be included in the differential diagnosis of gestating women with such symptoms to prevent delays in the diagnosis and treatment. Early detection and treatment of GTD are associated with a favorable clinical outcome. Considering the rare occurrence of CHM, we believe that accumulation of CHM cases by nationwide investigation is required to improve the diagnosis and management of this rare condition.

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完全性妊娠葡萄胎：一病例報告

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一位 15 歲未婚初次懷孕少女，因疑似罹患妊娠葡萄胎而經他院轉送本院。早在懷孕初期，已開始出現間斷性輕度子宮出血。當時，其血清人類絨毛膜性腺激素（hCG）達 91,816 mIU/ml。轉診本院後，更高達 1,407,359 mIU/ml，經陰道超音波發現子宮腔內有高回音囊狀妊娠腫塊，超音波像類似瑞士乳酪型狀，因此診斷為妊娠葡萄胎。據此診斷，給予子宮內容物刮除術，但未開立預防妊娠滋胚層腫瘤之化學治療藥物。手術後，無任何併發症。組織病理學報告證實為完全性葡萄胎。術後其 hCG 值穩定下降，且於術後 30 天達到正常值。術後 17 個月，她如願生下一位健康的足月女嬰。故針對年輕孕婦妊娠期前半段之胚胎疾病做鑑別診斷時，應想到是否有葡萄胎之可能性。及早診斷出葡萄胎並加以治療，有利於臨床之治療結果。

關鍵詞：妊娠葡萄胎、絨毛膜性腺激素、年輕孕婦

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Case Report

Trachway®-assisted Double-Lumen Endobronchial Intubation in a Patient with Limitation of Neck Motion: A Case Report

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Abstract

There are many options for managing the difficult airway. The video–light intubating stylet (Trachway®) is a device providing a direct view of the vocal cords (grade I view) in patients with difficult airways, particularly those with limitation of mouth opening. This device was designed for single-lumen endotracheal tube insertion. We used a modified intubation technique using a Trachway®-assisted double-lumen endobronchial tube in a patient with limitation of neck motion.

Key words: Double-lumen endobronchial tube insertion, difficult airway, Trachway®, C-spine spondylolisthesis

Introduction

Double-lumen endobronchial tube (DLT) insertion is a method for lung ventilation[1]. It cannot be replaced by a bronchial blocker in certain circumstances. Placement of DLT may be challenging in patients with difficult airway because of anatomic factors and the larger external diameter of the DLT[2]. We present a modified technique of DLT insertion using Trachway® assistance in a patient with spondylolisthesis of the C-spine and myelopathy.

Case Report

A 66-year-old man (height, 160 cm; weight, 46 kg) presented with frequent hiccups and mild difficulty in swallowing for 1 year. Contrast-enhanced chest computed tomography revealed circumferential mucosal thickening, 6.5 cm in length and 0.9 cm in thickness, in the middle to lower third of the esophagus. This was later confirmed to be esophageal squamous cell carcinoma, Stage cT3N0M0, for which he was scheduled for an esophagectomy.

He had type 2 diabetes mellitus for 10 years, controlled with regular medication. A cervical spine X-ray revealed grade I spondylolisthesis at the C5 level 2 years prior; however, the patient did not seek further evaluation or treatment. At the preoperative visit, we observed muscle weakness (muscle power grade 4) and thenar muscle atrophy of the corresponding dermatomal level on both hands. Neck motion was slightly limited; neck extension was limited due to neck pain on motion. Left-sided Spurling test resulted in numbness of the corresponding dermatome, but it was not present consistently. Airway examination showed a 40mm mouth opening, normal thyromental distance, and Mallampati grade II.

Due to limitation of cervical spine motion, a 35-Fr, left-sided double lumen endobronchial tube insertion was assisted using a video-light intubation stylet (Trachway®)(Biotronic Instrument Enterprise Ltd., Tai-Chung, Taiwan). The DLT was prepared by creating a three-sided, C-shaped incision at the 31-cm mark using of a scalpel. Each side of the

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incision was approximately 0.7 cm in length; in this manner, an opening flap with an area of 0.5 cm^2 was created at the lateral side of the bronchial lumen. The Trachway® was lubricated using 2% lidocaine jelly and inserted into the bronchial lumen through the created opening (Fig 1) to visualize the bronchial cuff, as shown in Fig 2.

Perioperative monitors included electrocardiogram, arterial line, and peripheral oxygen saturation. After pre-oxygenation with 100% oxygen through a facemask for 5 min, anesthesia was induced with 100 µg of fentanyl, 10 mg of cisatracurium, and 150 ml of propofol with 20 mg of lidocaine. Manual jaw thrust ventilation while using a facemask was provided until muscle relaxation occurred. The prepared DLT was inserted successfully with the assistance of Trachway®; laryngoscopic view was Cormack–Lehane grade I and intubation was performed by Trachway®-assisted DLT. After intubation, the improvised hole was sealed with Tegaderm™ (3M Health care) to prevent air leakage. Correct DLT placement was verified using a stethoscope and it was fixed at the 29-cm mark at the level of the incisors.

Discussion

Lung isolation is generally achieved using DLT or bronchial blockers[1,3] and neither is considered superior than the other[4]. These two devices are not always available in all hospitals. DLT is more difficult to insert than a single-lumen endotracheal tube (ETT), even in patients with normal airways, owing to the greater external diameter and structure of DLT[5]. The recommendations in the difficult airway algorithm of the American Society of Anesthesiologists were designed for single-lumen ETT. Therefore, the problem of inserting a DLT in the difficult airway may have more technical problems[6]. Some techniques of improving DLT insertion in difficult airways have been suggested, such as using the Bullard laryngoscope®(Circon) [5], GlideScope®[7], Fiberoptic Laryngoscopy WuScope®[8], video fiberoptic bronchoscope[9], Cook_ Airway Exchange Catheter®[10], and modified Trachlight® technique[11]. However, applicability of these methods is debatable because each method is suitable for only a particular condition of difficult airway.

Difficult airway can be caused due to difficult ventilation or difficult intubation. Awake fiberoptic bronchoscope-guided intubation is the gold standard for patients with difficult ventilation[1]. However, the fiberoptic bronchoscope may not be a good option for the hard and long DLT in a situation of difficult intubation. The relatively short fiberscope is difficult to manipulate with a long DLT. Moreover, the diameter gap between the fiberscope and DLT could cause difficulty in tube advancement, possibly causing vocal cord injury. Furthermore, the expensive and fragile fiberoptic bronchoscope may be damaged when used to facilitate DLT insertion.

Chen et al. reported a modified technique for DLT insertion through the difficult airway using Trachlight®[11]. This method has several advantages in managing difficult intubation due to poor direct visualization and presence of blood or secretions, and it

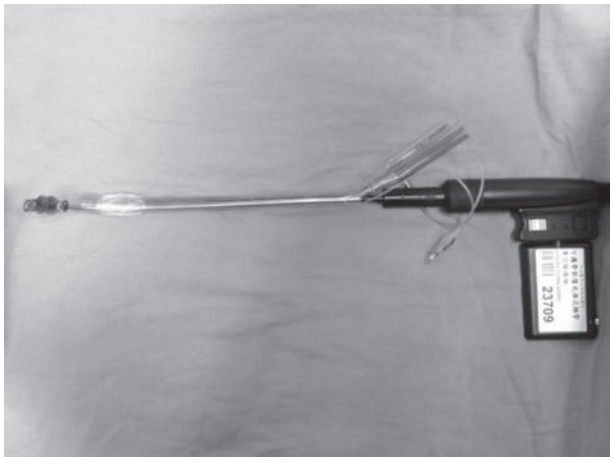

Fig. 1 Lubricated Trachway® was inserted into the bronchial lumen at the 31cm mark via the 0.5cm^2 window on the lateral side.

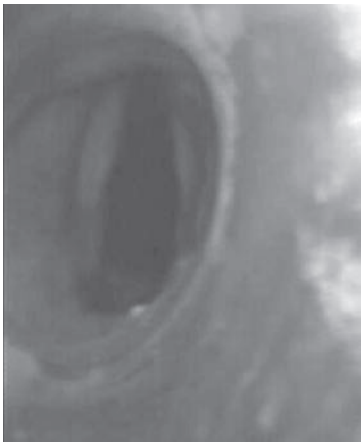

Fig. 2 Grade I view seen under Trachway®, the bronchial cuff could also be seen on the monitor.

is less invasive than retrograde intubation. However, Trachlight® is a device that enables insertion of the ETT without visualization of the laryngeal structures. Therefore, there is a potential risk for upper airway trauma[12]. Moreover, the learning Trachlight® use is difficult.

In our patient with limitation of neck motion, Trachway® provided a better alternative for DLT insertion compared with fiberoptic bronchoscope and Trachlight®. Trachway® can be used in patients with difficult intubation, such as those with limitation of mouth opening, poor dental situation, limitation of cervical spine range of motion, and other situations of difficult airway, except difficult ventilation. It has the advantages of both fiberoptic bronchoscope and Trachlight®. It could also be used as a Trachlight®. The stiff and curved stylet could easily advance the DLT to the aimed bronchus. It is easy to learn and manipulate even for an intern. Finally, the stylet can pass through a bronchial lumen with a size larger than 35 Fr. However, the stylet cannot pass through a bronchial lumen smaller than 32 Fr and correct DLT placement cannot be confirmed without a stethoscope or fiberoptic bronchoscope.

In the modified technique previously reported [11], a 2-cm^2 opening was created on the DLT just above the point where the bronchial pilot tube is connected. However, this position of the 3-sided opening flap should be made on the lateral side at the space between the 29- and 31-cm marks, just above the point where the bronchial pilot tube connects. If the opening flap is made below the 29cm mark, it may cause the problem of air leakage. In addition, there may be a risk for cutting off the pathway to balloon inflation. To overcome these limitations and accommodate the 5-mm external diameter of the Trachway®, we prepared the DLT, as described above, such that a 0.5-cm^2 opening flap was created for insertion of the Trachway® stylet. The advantage of the opening flap was that we could cover it with Tegaderm™ to prevent a possible air leakage.

In conclusion, Trachway® is a highly simple and useful device for patients with difficult airways. It could be a good device to assist DLT insertion in these patients; however, it may not be suitable for patients with difficult ventilation. The stylet cannot pass through bronchial lumen smaller than 32-Fr and we cannot confirm the position without a stethoscope or fiberoptic bronchoscope.

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頸椎活動受限之病患使用 Trachway 進行雙腔支氣管導管置放：案例報告

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摘要

Trachway 是許多困難插管工具中的其中一種，它能提供相當良好的插管視野，特別是在張口困難的病患身上。這項工具原本是設計用於一般氣管內管置放，但我們將它運用在張口困難或頸椎活動受限的病患來實行雙腔支氣管內管置放。

關鍵詞：雙腔支氣管導管置放、困難氣道、Trachway、頸椎滑脫

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Case Report

Utility of the Trachway® Intubating Stylet in Awake Orotracheal Intubation of Patients with Cervical Spine Disorder: A report of two cases

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Abstract

Awake intubation is generally performed using the fiberoptic method via the nasal route. However, oral intubation is the preferred option in patients with nasopharyngeal tumors or coagulopathy or those in the prone position. Here we used the Trachway® intubation stylet for awake orotracheal intubation. The first case was a patient with nasopharyngeal carcinoma and cervical spine disorder, whereas the second case was a patient with cervical spine disorder scheduled to receive lumbar laminectomy. Using the Trachway® intubation stylet, we could prevent massive nasal bleeding and facial pressure sores in both the cases.

Key words: Awake intubation, Nasopharyngeal neoplasms, Trachway®

Introduction

Awake intubation is indicated in patients with cervical spine instability undergoing surgery in the prone position. Once conscious and able to communicate, patients are repositioned to protect the cervical spine. Fiberoptic nasal intubation is a standard awake intubation method; however, it may cause tumor bleeding in patients with nasopharyngeal cancer, and nasal endotracheal tubes may produce severe pressure sores in patients in the prone position. Furthermore, nasal endotracheal tube may cause massive nasal bleeding in patients with severe coagulopathy and central nervous system infection or trauma in those with skull base fractures. Awake intubation by laryngoscopy is relatively challenging in cases with poor dental health or biting in response to pain stimulation. Irritability in response to pain may increase risk of cervical spine injury. Fiberoptic oral intubation is another potential option in such cases; however, it requires a skilled operator.

Here we used the Trachway® intubating stylet (Biotronic Instrument Enterprise Ltd., Taichung, Taiwan, R.O.C.) to perform awake orotracheal intubation, which is less painful than intubation via the nasal route and can easily be performed under relatively small mouth opening created using a bite block. Under light sedation and analgesia, patients could communicate using simple hand gestures, and we could reduce the risk of cervical spine injury and increase patient tolerance throughout the procedure.

Case Report

The first patient was a 43-year-old man (weight, 61 kg; height, 171 cm; body mass index, 20.86 kg/m^2) diagnosed with a C7 neurogenic tumor. Neurological

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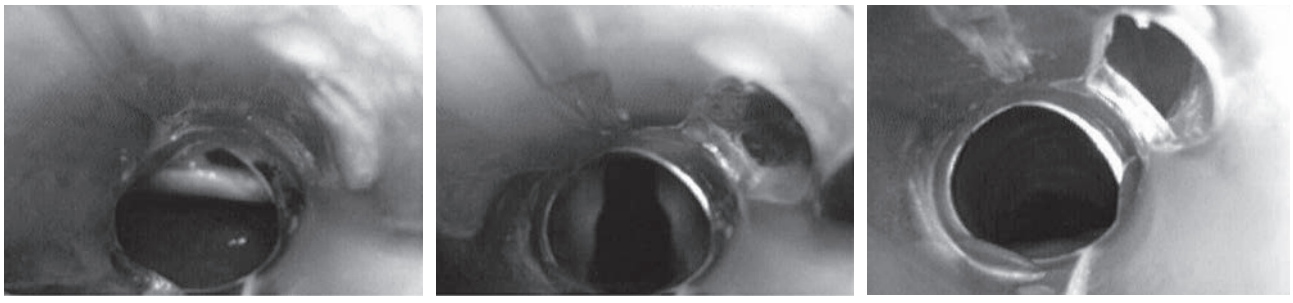
examination revealed left-sided upper limb paresthesia accompanied by decreased muscle strength on the left side and an unsteady gait. Thus, the patient was scheduled to undergo tumor excision and laminectomy for decompression. Comorbidities included nasopharyngeal carcinoma post chemotherapy and radiotherapy. Airway assessment revealed Mallampati class III with a limited mouth opening of 3 cm and a thyromental distance of 6.5 cm. Neck pain with limited range of motion was noted. Awake intubation was indicated because of a difficult airway and suspected cervical spine instability. However, there was concern regarding massive nasal tumor bleeding; therefore, we decided to use the Trachway® intubation stylet for awake orotracheal intubation[1,2,8-10].

The second patient was a 53-year-old man (weight, 70.75 kg; height, 164.0 cm; body mass index, 26.30 kg/m^2) diagnosed with L3-4, L4-5, and L5-S1 herniated intervertebral discs and scheduled to undergo laminectomy. The symptoms included persistent lower back pain with left-sided lower limb paresthesia and pain. Cervical spinal cord stenosis with limb paresthesia was also diagnosed. Airway assessment revealed Mallampati class III with a limited mouth opening of 3 cm and a thyromental distance of 6 cm. The surgeon requested that the patient be in the prone position for surgery; therefore, a nasal endotracheal tube was likely to have caused facial pressure sores during this procedure. Because direct laryngoscopy for tracheal intubation is difficult in patients with cervical spine disease[3],we decided to use the Trachway® intubation stylet for awake tracheal intubation.

Prior to intubation, we explained the entire procedure of awake intubation and repositioning to the patients. Patients were then asked to use hand signs to indicate neck pain or discomfort prevent further cervical spine injury. The patients were placed in the supine position for preoxygenation and both patients underwent transtracheal block with 2% Lidocaine (4 ml) and the administration of 10% Lidocaine spray to the oropharynx for local anesthesia. Atropine (0.5 mg) was administered intravenously to reduce secretions and Lidocaine (50 mg) was administered intravenously to inhibit the cough reflex. Midazolam (1 mg) and Fentanyl (50 μg) were administered for light sedation, followed by 0.5 mg of Midazolam titrated carefully to maintain adequate consciousness. A total of 2 mg and 2.5 mg of Midazolam was administered for sedation in the patients. The neck was positioned in the neutral position for both patients. After placing an oral bite block, we performed thorough suction of secretions and then the Trachway® intubation stylet with an endotracheal tube was advanced through the oropharynx and larynx under visualization on a monitor. The stylet was maintained in the midline of the oropharynx and advanced slowly. Following visualization of the epiglottis, the tip of the stylet was carefully advanced underneath the epiglottis and the vocal cords were identified. The tracheal tube with the stylet was slowly advanced through the glottis and then the endotracheal tube was advanced into the trachea (Fig. 1). The stylet was then removed with the endotracheal tube left in position. Jaw thrusts and neck movements were not required during intubation. Both the patients had a mild cough reflex but could still communicate with the anesthesiologist using simple hand gestures.

After endotidal CO_2 monitoring in the first patient, the endotracheal tube was fixed and then the patient was repositioned in the prone position with careful monitoring of the patient's gestures and



(A) (B) (C)

Fig. 1 (A) Visualization of the epiglottis. (B) Underneath the epiglottis, vocal cords were identified. (C) After passing through the glottis, tracheal cartilages were identified.

any signs of neck pain. After rechecking the position, the patient's head was fixed using a Mayfield skull clamp after administration of the local anesthetic. Finally, 50 mg of Propofol and 10 mg of Cisatracurium were administered. No further signs or symptoms of further cervical spine injury were observed during intubation and repositioning. The second patient was repositioned under careful observation of the patient's gestures following monitoring of endotidal CO_2 and fixing of the endotracheal tube. After the final check, 100 mg of Propofol and 10 mg of Cisatracurium were administered.

Discussion

Tracheal intubation in patients with cervical spine instability can be difficult. Awake fiberoptic nasal intubation is considered the ideal approach because it is safe and does not require neck movement. However, there are certain relative or absolute contraindications to nasal intubation including nasopharyngeal tumors, coagulopathy, and requirement to be in prone position for the surgery.

Several intubation tools are available for awake orotracheal intubation, such as fiberoptic intubation and the Pentax Airway Scope (AWS). However, successful fiberoptic orotracheal intubation requires high levels of technical skill and experience because of the sharp angle from the oral cavity to the oropharynx and interference by the tongue[11]. The Pentax Airway Scope (AWS), a video intubation laryngoscope, requires a larger space in the oral cavity and a wider mouth opening[4]. We used the Trachway® intubation stylet as our orotracheal intubation tool because it is technically easy to operate and can be used in patients with limited mouth opening[8-10]. The most common problems with the use of the Trachway® intubation stylet are excessive secretions and patient biting; therefore, thorough oral cavity suction and an oral bite block use are important. In addition, an anticholinergic agent aids in reducing secretions and facilitating intubation. Intravenous lidocaine is effective in reducing the cough reflex and attenuating the cardiovascular response to intubation[5-7].

To the best of our knowledge, this is the first case report describing the utility of the Trachway® intubation stylet in awake intubation of patients with cervical spine instability. The Trachway® intubation stylet causes lesser laryngeal stimulation and smaller mouth opening than a laryngoscope; in addition, it requires no neck movement. The findings of this report indicate that the Trachway® intubation stylet represents an additional option for awake intubation and can benefit patients undergoing surgery in the prone position.

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使用 Trachway® 於不適合經鼻內視鏡插管之病人進行清醒插管

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摘要

清醒插管最常使用的方式是經鼻內視鏡插管，但是在某些特殊情況下，經口插管會是較好的選擇，例如：同時有鼻咽癌、凝血機能異常，或是必須採俯臥姿勢進行手術的病患。本案例報告中，我們使用 Trachway® 進行經口清醒插管。第一位病患同時具有頸椎病變以及鼻咽癌，第二位病患則是有頸椎病變者預計進行腰椎椎板切除術。於此兩位患者，利用 Trachway® 插管可分別避免大量鼻腔內出血以及臉部壓瘡的併發症。

關鍵詞：清醒插管、鼻咽癌、Trachway®

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Case Report

Large-Diameter Patent Omphalomesenteric Duct with Omphalitis in a Premature Female Infant

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Abstract

The omphalomesenteric duct(OMD), also known as the vitelline duct, is a tube that connects the yolk sac and the midgut lumen in the developing fetus. Normally, it appears at the end of the fourth week of gestation and obliterates completely at approximately the ninth week of gestation. A persistent patent OMD (POMD) may cause result in the drainage of intestinal contents through the umbilicus, leading to local erythema, omphalitis, or even sepsis in premature infant. Here we present the case of a 10-day-old premature female infant with POMD that was repaired through a semicircular infraumbilical incision without the excision of the umbilicus or umbilicoplasty. Our experience with the case indicated that preserving the umbilicus using a semicircular infraumbilical incision without excision of the umbilicus or umbilicoplasty is suitable for treating POMD.

Key words: Patent omphalomesenteric duct; Omphalitis

Case Report

A 10-day-old premature female infant, born at 34 weeks gestation with a birth weight of 2500g was brought to the emergency room with the chief complaint of sudden passage of stool through the umbilicus. Physical examination revealed- local erythema of the umbilicus and granuloma formation. No obvious remnants of the umbilical vessels were found, except for a umbilical stump and semiliquid bile-stained discharge through the umbilicus. In addition, some brown fecal discharge from the umbilicus was found on the infant's diaper. Laboratory findings revealed mild leukocytosis and thrombocytosis. Although she was afebrile, she was admitted to the sick baby room for initial antibiotic treatments as a result of a preliminary diagnosis of omphalitis and POMD.

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Two days later, the umbilical erythema improved dramatically; however, the fecal discharge persisted. Following catheterization of the umbilical cord with an 8-F feeding catheter (Fig. 1), fluoroscopy with water-soluble contrast media revealed an omphalomesenteric fistula connected to the ileum (Fig. 2) confirming the diagnosis of POMD. On postnatal day 12, surgical repair was performed. After a downward curvilinear right-paraumbilical incision was made, the POMD was separated from the umbilical skin and the ileum was exposed through the incision. The junction between the POMD and ileum was identified, revealing that the diameter of the lumen of the POMD lumen was greater than that of the lumen of the ileum, which formed a pouch-like structure on the mesenteric side (Fig. 3). POMD excision, segmental ileal resection and anastomosis were performed. No additional suture was required after the closure of abdominal fascia(Fig. 4). The postoperative course was uneventful, and oral feeding was resumed three days after surgery. The patient was discharged on postoperative day four.

Discussion

The OMD is an embryonic structure that connects the yolk sac and the midgut in utero. Normally, the OMD obliterates completely between the fifth and ninth week of gestation. Failure of complete obliteration results in various OMD remnants including Meckel' s diverticulum, POMD, fibrous band, sinus tract, umbilical polyp and cyst. Meckel' s diverticulum is the most common remnant, reported in 2%-4% of the population in literature. A large-diameter POMD or fistula, as seen in our case, is rare, and spontaneous closure is unlikely.

In the literature, three main surgical techniques are reported for POMD repair: 1) a circular incision around the umbilicus with excision of the umbilicus and umbilicoplasty (T.Hasegawa et al.). 2) a semicircular infraumbilical incision without excision of the umbilicus and without umbilicoplasty (Sheth), and 3) a circular incision around the umbilicus also without umbilicoplasty (Flemming et al.). The choice between wedge resection and segmental resection depends on whether residual ectopic mucosa is present. The semicircular infraumbilical incision can be used as an alternative to umbilical resection for cosmetic reasons. This is because this method allows maintenance of good oxygenated blood circulation without

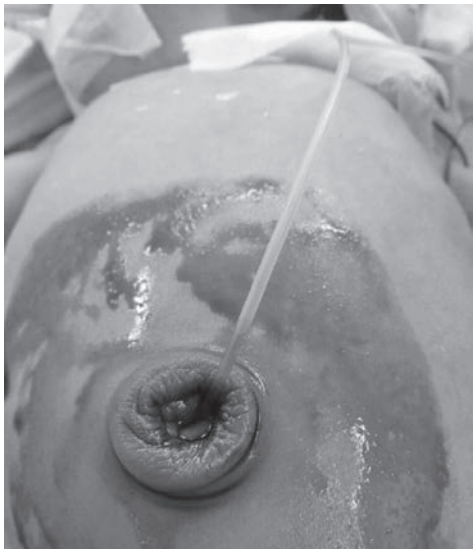

Fig. 1 A 8 Fr. feeding catheter was inserted into the patent omphalomesenteric duct(POMD).

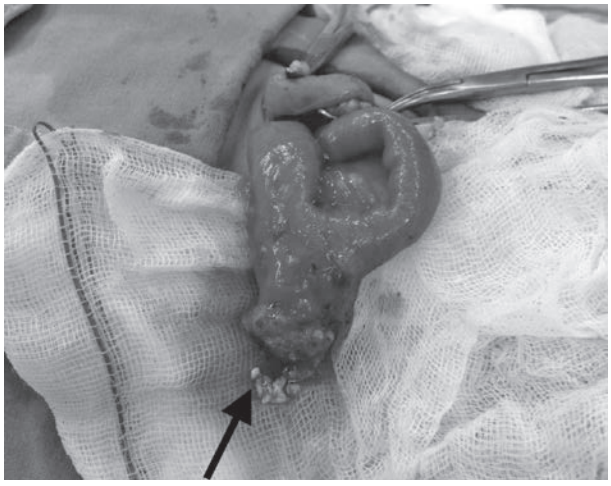

Fig. 3 The patent omphalomesenteric duct was dissected from the abdominal cavity : and the patent omphalomesenteric duct lumen(black arrow) was greater than the lumen of the ileum.

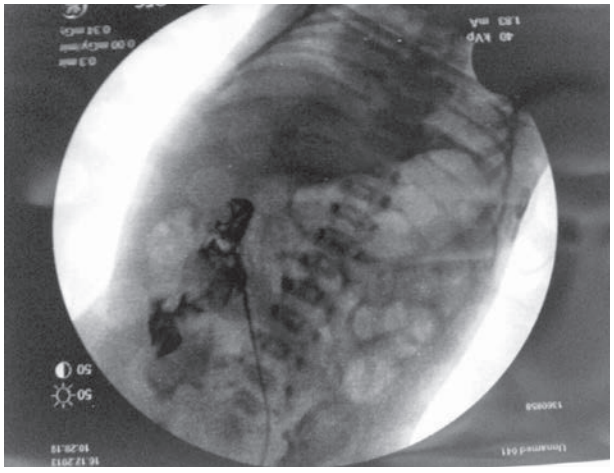

Fig. 2 Fistulogram showed the omphalomesenteric duct connecting to ileum.

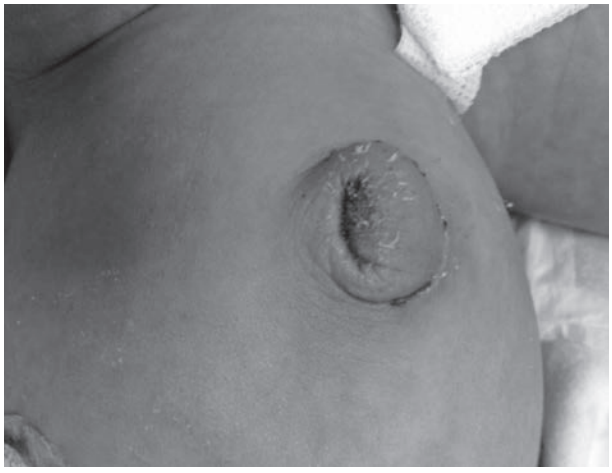

Fig. 4 Appearance of the umbilicus was preserved after operation.

destroying the original umbilicus and is, therefore, more esthetically pleasing.

Conclusion

In our case, spontaneous obliteration of POMD was unlikely. Surgical resection is a safe method for treating POMD. In our experience, preserving the umbilicus using a semicircular infraumbilical incision without excision of the umbilicus or umbilicoplasty is suitable for POMD.

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一個患有大直徑開放性臍腸系膜導管合併臍炎的早產女嬰

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摘要

臍腸系膜導管也被稱為卵黃管，是連接發育中的胎兒卵黃囊與中腸。它出現在胚兒期第四個星期結束時，並會約在第九週完全消失。一個存留的開放性臍腸系膜導管（POMD）在早產嬰兒，可能會導致腸內分泌物會從臍流出，引起局部紅斑，臍炎甚至敗血症。本文報告一年齡 10 日的早產女嬰患有（POMD），接受臍部保留手術治療後順利恢復。

關鍵詞：開放性臍腸系膜導管、臍炎

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Case Report

A Case Report on Hemimegalencephaly

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Abstract

Hemimegalencephaly (HME) is a rare disorder thought to occur because of insults during the second trimester of pregnancy or as early as the 3rd week of gestation. HME may be an isolated finding or be associated with genetic syndromes with various clinical presentations. Diagnosis of HME may be clinically made in syndromic cases, whereas brain imaging is required in isolated cases and for prenatal diagnosis. In general, the brain surface may show pachygyria and polymicrogyria. Microscopically, the nerve cells are larger and less densely packed than that in the normal side of the brain, and the number of glial cells is increased. Here we report a case of a female infant with intractable focal seizures with facial dysmorphism and developmental delay. T1 weighted images of the magnetic resonance imaging scan of the brain showed a moderately enlarged left cerebral hemisphere with broadened gyres and a diffusely thickened cortical mantle. These findings are compatible with isolated forms of HME.

Key words: Hemimegalencephaly, Pachygyria, Polymicrogyria

Introduction

Hemimegalencephaly (HME) is a rare brain malformation that involves overgrowth of one hemisphere of the brain[1] and was first described by Sims in 1835 after reviewing 253 autopsies.[2] Although the cause is unknown, it is postulated that HME occurs because of insults during the second trimester of pregnancy or as early as the 3rd week of gestation, as a genetically programmed developmental disorder related to cellular lineage and establishment of symmetry.[2] HME may be an isolated finding or be associated with epidermal nevus syndrome, Proteus syndrome, encephalocraniocutaneous lipomatosis, hypomelanosis of Ito, Klippel-Trenaunay syndrome, and tuberous sclerosis complex.[1] Clinical presentations vary from some degree of mental retardation, intractable epilepsy, contralateral hemiparesis, and hemianopsia to near normal neurological development.[1]

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Case presentation

A 7-month-old girl presented with intractable attacks of right-sided focal seizures. She was the second child of healthy, non-consanguineous parents; she was born at 38 weeks gestation via normal vaginal delivery, weighed 3000 g, and had no known perinatal insults. She was developmentally delayed, and developmental evaluation revealed delays in fine and gross motor development (poor head control, partial roll over, and unstable sitting with support), in cognitive/language development (ability to say "ah-ah," no response to name with head turning, and ability to make eye contact and smile), and in psychosocial development (could not discriminate between strangers and family members, e.g., frowns, cries, and absence of stranger/separation anxiety). No additional clues could be gained from the family history.

Upon admission, a physical and neurological examination revealed that the girl had an acute ill-looking appearance and a clear consciousness. Her body weight was 8 kg (below the 60th percentile) and her height was 68 cm (below the 50th percentile). Her head circumference was enlarged and measured 47.4

Imaging findings

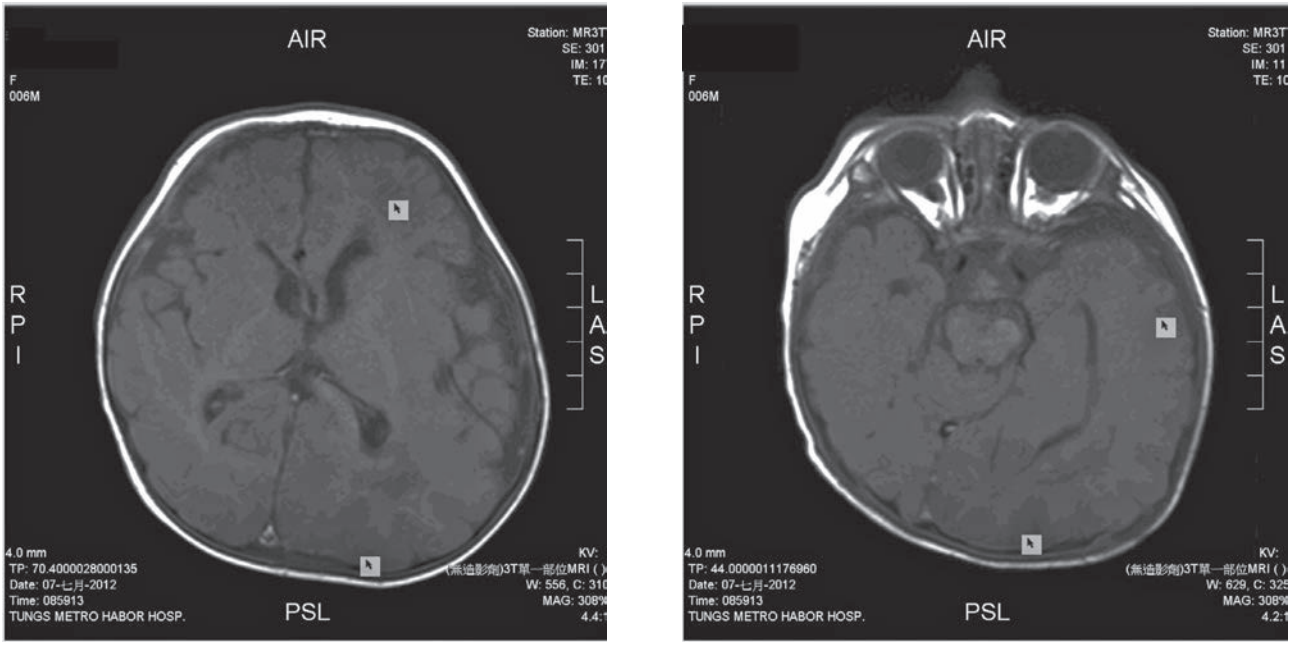

Fig. 1 T_1-weighted magnetic resonance image (MRI) images showing a moderately enlarged left cerebral hemisphere with broadened gyri and a diffusely thickened cortical mantle, consistent with areas of pachygyria and polymicrogyria (arrow head). The left lateral ventricle was dysmorphic with portions that were compressed.

cm (97th percentile). Her blood pressure was 80/50 mmHg.

Further examination revealed left facial hemihypertrophy. Her cranial nerves were intact, but both muscle tone and deep tendon reflexes were mildly increased on the right side. The patient had right-sided hemiparesis and no cutaneous abnormalities. Her pupils were isocoric with normal light reflexes, her eye movements were unimpaired, and no nystagmus was found. An eye fundus examination revealed no abnormalities. Laboratory data showed a normal hemogram. The results of liver and renal function tests and a cerebrospinal fluid (CSF) test were normal. Arterial blood gas analysis revealed a pH of 7.439, oxygen pressure (PaO_2) of 106.8 mmHg, and bicarbonate (HCO_3) was 21.7 mmol/L.

After admission, several brain scans were performed. The patient underwent a magnetic resonance imaging (MRI) scan of the brain, which showed marked enlargement of the left cerebral hemisphere and findings consistent with HME (Fig 1). The left cerebrum was diffusely dystrophic with broadened gyri and a diffusely thickened cortical mantle, consistent with areas of pachygyria and polymicrogyria. The left lateral ventricle was dysmorphic, with portions that were compressed (Fig 2). The left globus pallidus, putamen, and thalamus were poorly demarcated, and the corpus callosum was small (Fig 2). The cerebellum and brainstem appeared normal. The right cerebral hemisphere had a more normal gyral pattern; however, there were regions of thick gray matter and pachygyria in the right frontal lobe, consistent with cortical dysplasia. These imaging findings were consistent with left-hemisphere HME. An electroencephalogram showed a fast beta rhythm in the left cerebral hemisphere (Fig 3)

To treat the patient's seizures, she was initially administered phenobarbital. Although initially responsive to antiepileptic treatments, the patient continued to experience seizures during the following few weeks, despite optimal administration of phenobarbital. The seizures were subsequently well-controlled with topamax (8 mg).

At the age of 1 year, 2 months, the patient remained under follow-up surveillance at the outpatient department. Her seizures were well-controlled with topamax (topiramate; Ortho-McNeil Pharmaceutical, Raritan, NJ, USA) and phenobarbital. Her developmental progress improved, as she reached further milestones, including improvements in gross

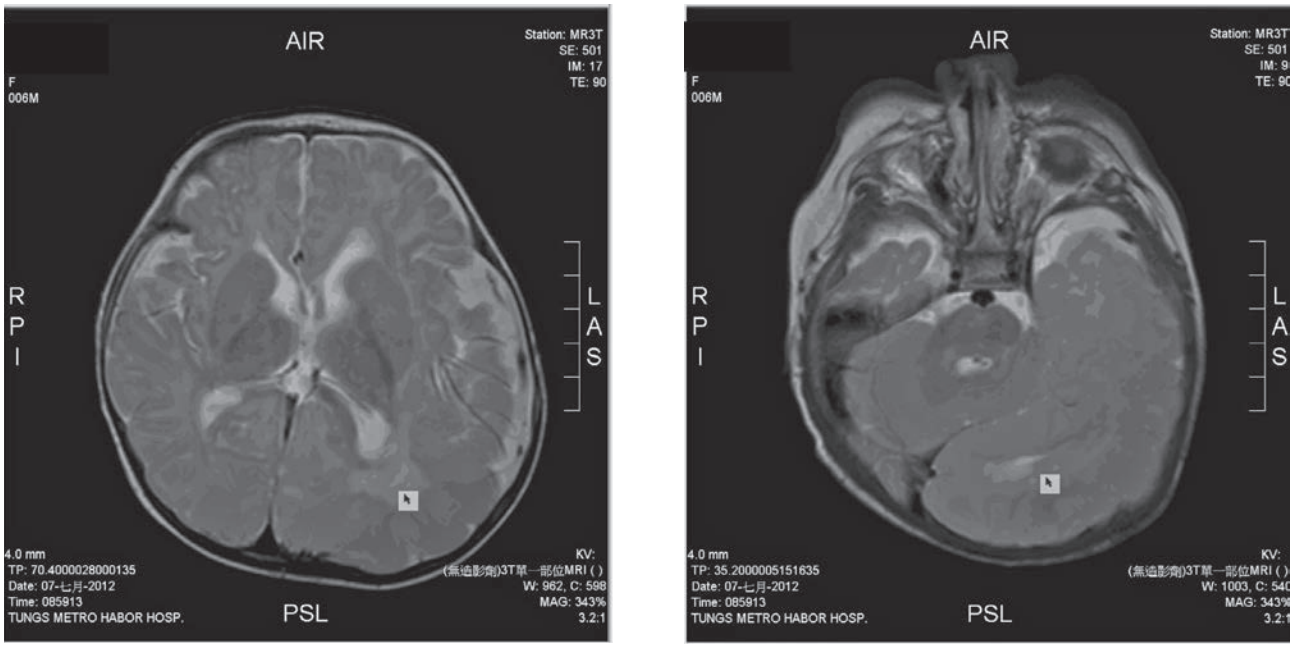

Fig. 2 T_2-weighted magnetic resonance image (MRI) showing a moderately enlarged left cerebral hemisphere with high signal intensity in the left periventricular white matter correlates with poor myelination (arrow head).

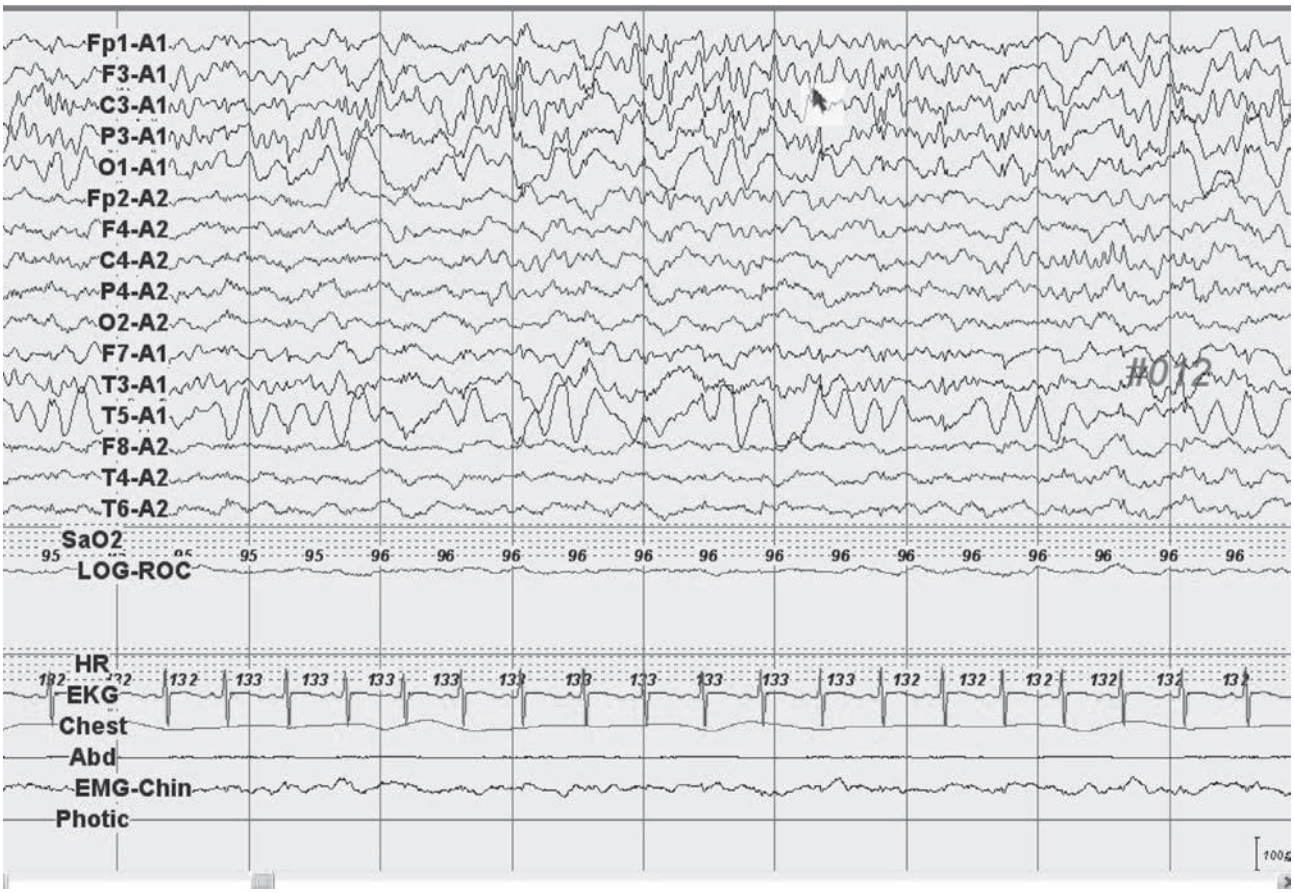

Fig. 3 The electroencephalogram showed fast beta rhythm in the left cerebral hemisphere (arrow head).

and fine motor skills, such as being able to roll over on both sides, approaching objects, sitting unassisted, and ability to speak simple syllables like "pa, pa" and "ma, ma").

Discussion

HME is a nonfamilial congenital brain malformation involving overgrowth of a part of one hemisphere, an entire hemisphere, or one whole hemisphere and part of the other.[1] To date, no chromosomal abnormalities have been associated with HME.[2] There are three types of HME. The isolated form, as observed in the present case, occurs as a sporadic disorder without hemicorporal hypertrophy or cutaneous or systemic involvement. Second, the syndromic form is associated with other diseases and may occur as hemihypertrophy of part or all of the ipsilateral body. This form has been described in patients with many different types of syndromes, and may follow a Mendelian pattern of inheritance. The third and least common type is total HME, in which there is also enlargement of the ipsilateral half of the brainstem and cerebellum.[2]

A diagnosis may be clinically made in syndromic cases, whereas brain imaging is required in isolated cases.[1] While both ultrasonography and MRI may be used to diagnose HME, MRI is generally preferred. Before birth, a prenatal ultrasound examination may reveal hydrocephalus and macrocrania. Additionally, a prenatal MRI may reveal ventricular enlargement and restricted diffusion, suggesting increased cellularity and advanced myelination in the affected hemisphere.[1] In neonates, cranial sonographic findings include an enlarged hemisphere, thickened lateral ventricle, thickened periventricular white matter with increased echogenicity, and displaced midline structures. Postnatal MRI generally reveals an enlarged cerebrum involving at least one lobe, with a thickened cortex; broad gyres; abnormal gray-white matter differentiation with abnormal signs; and neuronal heterotopia, ventricle asymmetry, basal ganglia, and internal capsule abnormalities.[1]

In addition to excessive growth limited to one cerebral hemisphere, MRI studies have revealed various other abnormalities accompanying this condition, such as enlargement of the lateral ventricle, an abnormal gyral pattern with a thick cortex, gliosis in the white matter on the affected side, and abnormal myelination,[4] as observed in the present case. Magnetic resonance spectroscopy (MRS) usually shows a decrease in glutamate, N-acetylaspartate, and creatine in the white matter, but less severe changes or no changes in the cortical gray matter. In the contralateral normal white matter, there was only a mild metabolic derangement.[1] These findings suggest the presence of irreversible loss or damage of neuroaxonal tissue.[1] EEG findings of the affected hemisphere included an asymmetric amplitude of the normal, age-related rhythms; slow, rhythmic, or fast activity; and multifocal unilateral or bilateral high-amplitude spikes and spike-wave complexes. There may be generalized or independent interictal bilateral discharges. In the first months of life, unilateral suppression burst pattern or hypsarrhythmia may be present.[1] Positron emission tomography and single-photon emission computed tomography revealed increased cerebral blood flow usually to the affected side.[1]

Seizure control is the principal goal of therapy, and patients often require multiple antiepileptic medications that have adverse side effects.[2] However, in the present case, the seizures were unexpectedly well-controlled with f topamax and phenobarbital If medications are unable to control the seizures, surgery may be required. Hemispherectomy was first performed for the treatment of refractory epilepsy in 1978 and is considered the best therapeutic choice for patients with intractable seizures.[2] Less aggressive surgeries, such as temporal lobectomy, resection of the central supra-sylvian cortex with disconnection of the frontal and occipital lobes, and complete callosotomy are currently being used.[1] More conservative surgeries with partial resection and less disconnection have not achieved good surgical control.[1] Complications of these surgeries have included subdural hematomas and hydrocephalus, often requiring surgical intervention and ventriculoperitoneal shunting.[2]

Conclusions

Hemimegalencephaly is a rare, nonfamilial congenital brain malformation which should be considered in patients with intractable seizures with facial dysmorphism and focal cortical abnormality as observed in an EEG scan. In this report, we describe the case of an infant girl, presenting isolated HME with

intractable focal seizures, facial dysmorphism, and developmental delay. Her MRI scan showed a moderately enlarged left cerebral hemisphere with broadened gyres and a diffusely thickened cortical mantle, findings that are compatible with isolated forms of HME. In this type of case, epilepsy is one the worst symptoms; and therefore, seizure relief is essential for neurological development. In the present case, the girl's seizures were successfully treated with a combination of topamax and phenobarbital. Surgery is often required when medications fail to achieve seizure control, but in this case, medication successfully avoided surgical intervention.

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半側巨腦症 - 病例報告

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摘要

半側巨腦症是一種罕見疾病。它最初由 Sims 在 1835 年提出，他假設造成的原因是妊娠第二期的損傷，亦或有可能早在懷孕第三週即造成損傷。它可以是單獨出現的疾患，或是與其他遺傳症候群中的許多臨床表現相關聯。在症候群的案例中，臨床症狀是主要的診斷方式，但在少數案例及產前的診斷則需要腦部影像學的檢查。外觀病灶，腦部表面主要呈現腦回平厚畸形及多小腦回畸形；在顯微鏡底下，呈現神經細胞較正常來的大且排列較不致密，而且神經膠質細胞的數目明顯增加。此篇文章我們報導一個半側巨腦症單獨出現的個案，是一位罹患頑固性局部癲癇的女性嬰兒，合併有臉部畸形及發展遲緩。大腦核磁共振影像的 T1 weighted images 中，顯現中等程度變大的左側大腦半球，與寬闊的腦回及廣泛增厚的大腦皮層。這些影像學的發現，都與單獨型的半側巨腦症相吻合。

關鍵詞：半側巨腦症、腦回平厚畸形、多小腦回畸形

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Tungs' Medical Journal 9 (2015) 142-145

Pathology Page

Adrenal Cortical Carcinoma: A case report and literature review

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Abstract

A 72-year-old female with hypertension received regular treatment at our cardiovascular outpatient department. After six years of treatment, she complained of left upper quadrant abdominal pain that had been occurring occasionally for five months. Sonography of the abdomen revealed a 5.6 cm left suprarenal mass. Furthermore, magnetic resonance imaging showed a large irregular heterogeneous left adrenal enhanced mass, measuring approximately 5.4 × 4.5 cm with central necrosis. Based on suspected pheochromocytoma, daVinci robotic-assisted laparoscopic en bloc resection of the left adrenal tumor was performed. Diagnosis of stage I (≤5 cm) adrenal cortical carcinoma (ACC) was made based on microscopic diagnostic criteria of Weiss score along with immunohistochemical stain findings (positive for Melan A and synaptophysin and negative for chromogranin). ACC is a rare malignant adrenal cortex tumor. Here we report an ACC case and review the literature.

Key words: Adrenal cortical carcinoma, pheochromocytoma

Pathology Page

A 72-year-old female with hypertension and DM received regular treatment at our outpatient department for six years. She complained of left upper quadrant abdominal pain that had been occurring occasionally for five months. Sonography of the abdomen revealed a 5.6-cm left suprarenal mass. Magnetic resonance imaging showed a large irregular heterogeneous enhanced mass in the left suprarenal region, measuring approximately 5.4 × 4.5 cm with central necrosis, probably arising from the lateral limb of the left adrenal gland. Based on these findings, pheochromocytoma was suspected. On admission, physical examination revealed a palpable mass with mild tenderness over the left upper quadrant abdominal region. The patient's blood pressure was 204/96 mmHg. Laboratory data were as follows: Na/K, 140/4.5 mEq/L; BUN/Cr/GFR, 25.8 mg/dl/1.3 mg/dl/42.8 ml/min/1.73 m^2; VMA, 33.8 mg/24 h (normal range, 1–7.5 mg/24 h); cortisol, 27.5 μg/day (normal range, 5–25 μg/day); aldosterone, 77.28 ng/dl (normal range, 3.7–24 ng/dl); renin, 3 ng/ml (normal range, 1.31–3.95 ng/ml); and aldosterone/renin, 25/76. Angiography of the left renal artery and left middle suprarenal artery showed a hypervascular tumor measuring 6.6 × 6.8 cm superior to the left kidney, which was supplied mainly by the left middle suprarenal artery. Transcatheter arterial embolization of the left adrenal gland was performed for preoperative vascular reduction. Because we suspected pheochromocytoma, da Vinci robotic-assisted laparoscopic en bloc resection of the left adrenal tumor was performed.

The tumor tissue measured approximately 6.5 × 4.5 × 4 cm in size and 70 gm in weight. The tumor was gray–yellow in color, well encapsulated with multifocal hemorrhage and necrosis, measuring around 5 × 3.9 cm in size. Residual adrenal gland tissue was also found in the focal periphery region (Fig. 1).

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Histopathology showed diffuse proliferation of cords, nests, sheets, and trabecular and serpiginous pattern tumor cells with eosinophilic bubbly cytoplasm and variable pleomorphic giant nuclei tumor cells (Fig. 2). Areas of confluent necrosis as well as capsular and vascular invasion were also found (Fig. 3). The mitosis rate was less than 5/50 HFP but abnormal mitosis was observed. Immunohistochemically, these tumor cells were positive for vimentin, synaptophysin, Melan A (Fig. 4), and negative for CK AE1/AE3, EMA, and chromogranin. Based on the histopathological and immunohistochemical (IHC) stain findings, stage I (≤5 cm) adrenal cortical carcinoma (ACC) was diagnosed and the Ki-67 proliferative index was 3%.

ACC is a rare (0.5~2 million cases per year) and aggressive disease. Sixty percent of all ACC patients present with hormone-related signs and symptoms (so called "functional tumors"); Cushing's syndrome with or without virilization is its most frequent presentation.[1, 2]

Although surgery is the mainstay of therapy and represents the only chance of cure, majority of the patients treated with radical resection (up to 80% in some series) are still destined to experience relapse, often with metastases.[1, 2]

Pathological diagnosis should be performed by

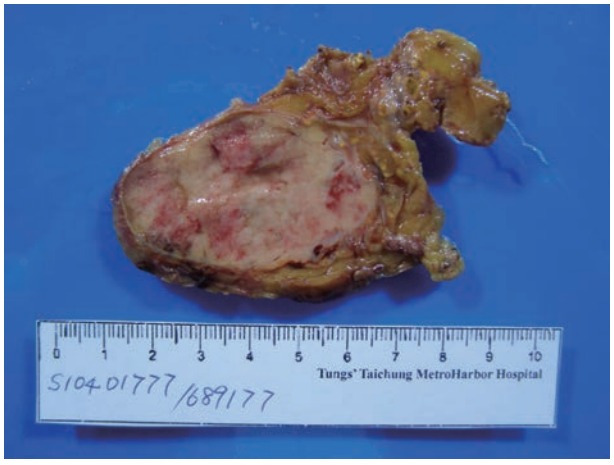

Fig. 1 The tumor mass showed yellow gray color, well encapsulated, multifocal hemorrhage, necrosis and measuring around 5 x 3.9 cm. The residual adrenal gland tissue is found in the focal periphery area(arrow).

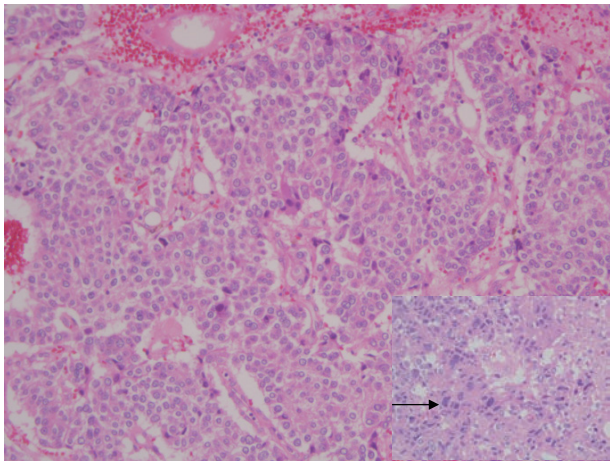

Fig. 2 Histopathology showed diffuse proliferation of sheets, trabecular and serpiginous pattern tumor cells with eosinophilic bubbly cytoplasm (H & E stain x 200)., and variable grade 4 pleomorphic nuclei tumor cells (arrow) (insertion panel, H & E stain, x 400).

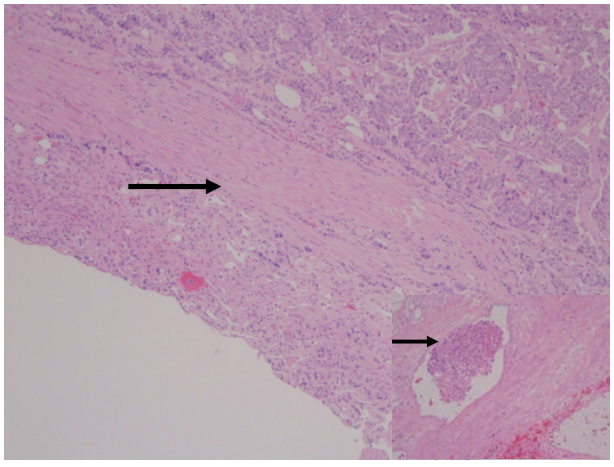

Fig. 3 Capsular invasion(long arrow) (H & E stain, x 100) and vascular invasion (short arrow) (insertion panel, H & E stain x 200).

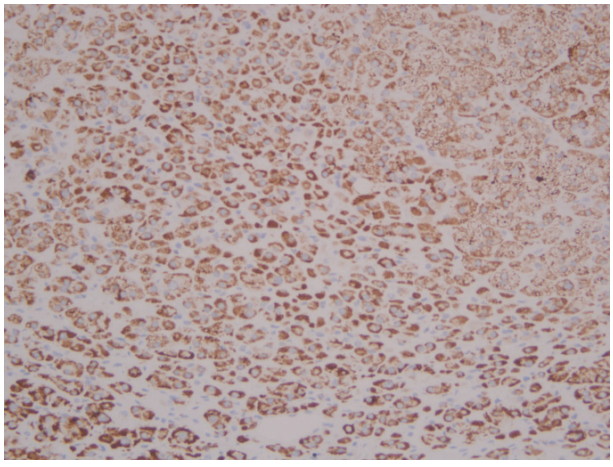

Fig. 4 Tumor cells are diffuse positive for Melan A immunostain (IHC stain x 200).

experts. Benign and malignant adrenal cortical tumor differentiation is difficult and is based on macroscopic and microscopic characteristics. Macroscopic findings, weight, hemorrhage, and tumor capsule and vascular invasions are evaluated. Weiss score is the most widely used classification method for microscopic characteristics suggestive of malignant tumor and enumerates nine histological criteria:[3]

1. High mitosis rate (>5 per 50 high field)
2. Atypical mitoses
3. Venous invasion
4. High nuclear grade (Fuhrman III to IV)
5. Absence of cells with clear cytoplasm (<25% of cells)
6. Diffuse growth pattern (more than a third of the tumor)
7. Confluent necrosis
8. Sinusoidal invasion
9. Capsular invasion

Three or more of these aspects are necessary for ACC diagnosis. Our patient showed seven aspects (including atypical mitosis, venous invasion, high nuclear grade, absence of cells with clear cytoplasm, diffuse growth pattern, confluent necrosis, and capsular invasion), leading to ACC diagnosis. Although pheochromocytoma (positive for synaptophysin and chromogranin and negative for Melan A) may appear to be histologically similar to ACC (positive for synaptophysin and Melan A and negative for chromogranin), we can use the IHC stains to differentiate between these two entities. The finding of pheochromocytoma is the most reliable evidence of malignancy.[5] According to the recent German ACC registry study, clinical outcomes differed significantly between patients with Ki67 <10%, 10%–19%, and ≥20% (for the German cohort: median progression-free survival 53.2 vs. 31.6 vs. 9.4 months; median overall survival, 180.5 vs. 113.5 vs. 42.0 months). Thus, evaluation of Ki67 indices should be introduced as standard grading in all pathology reports of ACC patients.[6] Our patient's Ki-67 proliferative index was 3%. In a European series of patients, the 5-year survival rates were 60% for stage I, 58% for stage II, 24% for stage III, and 0% for stage IV. Importantly, the median overall survival for metastatic disease (stage IV) at the time of diagnosis is less than one year. Approximately 80% of these patients present local or distant recurrence after complete resection.[3, 4]

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腎上腺皮質癌：一病例報告及文獻回顧

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童綜合醫院 [1]泌尿科 [2]病理部

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摘要

一位 72 歲女性有高血壓病史大約 6 年時間，並且在門診持續追蹤治療。病人抱怨最近 5 個月左上腹部會痛。門診腹部超音波檢查發現在左腎上腺有一 5.6 公分的腫塊，核磁共振檢查發現在左腎上腺有一 5.4 x 4.5 公分加強顯影的腫塊，中央部分有壞死現象。在臨床診斷為腎上腺嗜鉻細胞瘤下，病患接受經腹腔鏡達文西機械手臂協助左腎上腺腫瘤切除手術。依據 Weiss 顯微鏡下診斷條件以及免疫染色的結果）Melan A+, synaptophysin+ and chromogranin-），最後病理診斷為腎上腺皮質癌。腎上腺皮質癌是腎上腺皮質非常少見的惡性腫瘤，於此我們報告一病例並且做一文獻回顧。

關鍵詞：腎上腺皮質癌、腎上腺嗜鉻細胞瘤

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Tungs' Medical Journal 9 (2015) 146-148

Images

Primary Fibrosarcoma of Thyroid — A Rare Cause of Upper Airway Obstruction

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Abstract

Primary fibrosarcoma of thyroid is an uncommon thyroid malignancy which may potentially cause vocal palsy and upper airway obstruction. We herein report a case of thyroid fibrosarcoma encountered at the Department of Otolaryngology, Tungs' Taichung MetroHarbor Hospital and discuss its clinical presentation as well as treatment options.

Key words: Thyroid gland neoplasms, Fibrosarcoma

Fibrosarcoma is a malignant neoplasm of mesenchymal cell origin in which histologically the predominant cells are fibroblasts that divide excessively without cellular control; they can invade local tissues and metastasize to distant body sites. Fibrosarcoma consists 1-3% of sarcomas and has a predilection to occur in the lower extremeties[1]. Primary fibrosarcomas occurring in the thyroid is very rare.

A 71 years old male patient visited our ENT outpatient clinic at the end of June 2014. The patient had chronic kidney failure combined with cardiovascular and diabetic diseases. He was aware of the hoarseness in voice accompanying with the fast growing lump in the right neck within two weeks. Clinical examination observed an epiglottic tumor and a right vocal cord paralysis. In addition, a tumor of 8-9 cm in diameter was palpated in the right neck. The pathologic report from subsequent biopsies showed that the epiglottic tumor was a squamous papilloma and the neck tumor, a sarcoma. Because the patient was hesitant to undergo surgical treatment, he was then discharged from the hospital. Consequently, he was readmitted to our hospital two days later due to breathing difficulty caused by the displaced trachea and he received emergent tracheotomy. Computed tomography revealed several calcification spots (arrow) in the thyroid, which was suspected as the primary site of tumor. Total thyroidectomy and lymphadenectomy were performed in July 2014. Total surgical time was about seven hours, but the tumor could not be removed completely because it tightly circumferentially surrounded the internal carotid artery. Breathing problem was resolved after the removal of tumor and patient was sent to

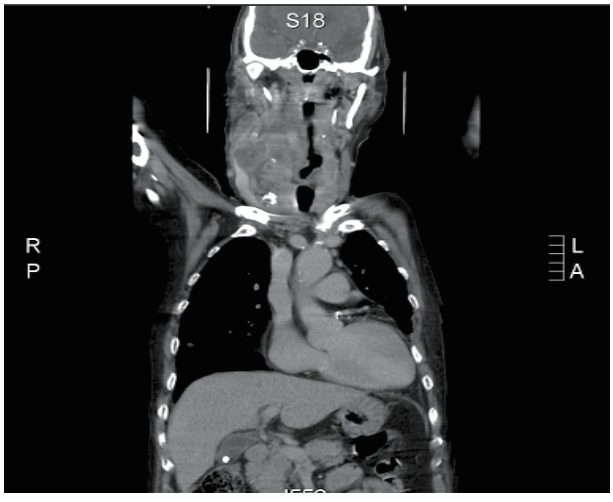

Fig. 1 Computed tomography shows several calcification spots (arrow) in the thyroid and the displacement of the trachea.

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the intensive care unit. The pathologic report identified the case as thyroid fibrosarcoma combined with goiter. Radiotherapy alone was given post-surgery because chemotherapy was unsuitable due to patient's poor renal function.

Fibrosarcoma is generally found in 50-60 years old male[2]. Fibrosarcoma rarely occurs in the thyroid and was not included in the new TNM staging of thyroid tumors. Patient usually has a rapid growing neck tumor with less distant metastasis, but the survival rate is not high. It often causes breathing difficulty. General treatment is combining chemotherapy with radiotherapy. However, when breathing difficulty is encountered, debulking surgery is also recommended first to clear the respiratory tract, followed by radiotherapy and chemotherapy [3].

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甲狀腺惡性纖維肉瘤—上呼吸道阻塞罕見的原因

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摘要

甲狀腺惡性纖維肉瘤是一不常見的甲狀腺惡性腫瘤，此腫瘤可能造成聲帶麻痺和上呼吸道阻塞。在此我們提出一例於童綜合醫療社團法人童綜合醫院耳鼻喉科治療的甲狀腺惡性纖維肉瘤，並討論此腫瘤的臨床表現與治療。

關鍵詞：甲狀腺腫瘤、惡性纖維肉瘤

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參、投稿須知

1. 稿件須符合「生物醫學雜誌投稿之統一規定」[1]，請以電腦隔行 double space 書寫，並編頁碼，中文字型以標楷體，英文字型以 Time New Roman 12 號字大小，稿紙之左右緣爲 2.54 公分，上下緣爲 3.17 公分。
2. 第一頁爲標題頁，須列出中文及英文之論文題目、中英文作者姓名、所屬機構及單位之中英文稱號（分屬不同單位，請以阿拉伯數字標出作者與單位）、聯絡人姓名、電話及中英文通訊錄。
3. 第二、三頁爲中文及英文之摘要及關鍵詞（請提供 3 至 5 個關鍵詞或簡短片語），中英文摘要須完全相同，摘要分段撰寫，依序爲背景及目的（Background and purpose）、方法（Methods）、結果（Results）及討論（Discussion）。
4. 相同貢獻作者請加註說明，如研究主題的設定、參與決定研究設計、進行統計分析、詮釋研究結果、以及各章節撰稿等貢獻。
5. 圖表應專業製作，一張紙僅一個附圖或附表，依引用順序以阿拉伯數字標出排列。附表須有標題及說明且不可以照片形式。圖片或照片電子檔（.jpg）必須清晰、分明。，附圖須有簡單說明（Legend），並另頁撰寫。光學或電子顯微鏡照片，請註明擴大倍率或比例。

註：[1] 根據「生物醫學雜誌投稿之統一規定」第五版，刊載於 Annals of Internal Medicine 1997;126(1): 36-47.

肆、參考文獻

未經發表之論文或摘要不得列爲參考文獻，但可於本文中說明並註明「未發表」（unpublished observations）。博碩士論文可引用。已被任何雜誌接受刊發但仍未發表之著作，請列出雜誌名稱及年份，並註明「in press」。

原著論文、病例報告、綜論、短論、影像判讀、臨床病理討論、編著的話按下列格式撰寫：

A. 雜誌及期刊

中文例〔作者姓名：題目。雜誌簡稱 年號；卷數：起訖頁數〕

薛玉梅、陳建仁：皮膚砷癌之流行性病學特徵與危險因子。中華衛誌 1996;15:1-26。

英文例〔英文原稿中引用的參考文獻，其雜誌或期刊之簡稱應參照 Index Medicus 型式〕

1. Feely J,Wilkinson GR, Wood AJ. Reduction of liver blood flow and propranonol metabolism by cimetidine. N Engl J Med 1981;304:691-6.
2. Kaplan NM. Coronary heart disease risk factors and antihypertensive drug selection. J cardiovasc Pharmacol 1982;4(suppl 2):186-365.（引用雜誌附冊時）
3. Tada A, Hisada K, Suzuki T, Kadoya S. Volume measurement of intracranial hematoma by computedtomography. Neurol surg (Tokyo) 1981;9:251-6.〔In Japanese: English abstract〕（引用文獻之作者之本文爲非英文，但有英文摘要）。
4. Bhasin S, Storer TW, Berman N, Callegari C, Clecenger B, Phillips J, et al. The effects of supraphysiologic doses of testosterone on muscle size and strength in normal men. N Engl J Med 1996; 335:1-7.（作者超過 6 位時，只須列出前 6 位，其它以「等」(et al) 代替）

＊期刊若有「數位物件識別碼 (digital object identifier, DOI)」，則於文獻末。

B. 單行本：

中文例 [作者姓名：書名，版數（卷數）。發行地；出版公司，年代：引用部份頁數]。

楊志良：生物統計學新論，一版。台北；巨流圖書公司，1984：33-8.

英文例 [英文單行本的書名，除介系詞及連接詞外，第一字母需大寫]

(1) Plum F, Posner JB. Diagnosis of Stupor and Coma. 3rd ed., Philadelphia: Davis, 1980:132-3.

C. 多重作者之單行本：

中文例 [有關文章作者姓名：題目 。編輯者姓名：書名 。版數（卷數）。發行地：出版公司，年代；引用部份頁數]。

蔣欣欣：護理與健康。顧乃平：護理專業導論。一版。台北：匯華出版公司，1991：83-121。

英文例 Levinsky NG: Fluid and electrolytes. In: Thorn GW, Adams RD, Braunwald E, lsselbacher K, Petersdprf RG eds. Harrison’s Principles of Internal Medicine. 8th ed. New York: Mcgraw-Hill, 1977;364-75.

D. 參考文獻引用時，若兩名以下作者請列出姓氏。兩名以上則列出第一名之姓氏，其他以「等」(et al) 代替，並以阿拉伯數字方括弧表示於引用之後。

例：One of the first well documented reports of ECH poisoning with fatality in young children was reported by Miller et al. in 1970[2].

伍、著作權

若著作人投稿於本刊經收錄後，同意授權本刊得再授權國家圖書館或其他資料庫業者，進行重製、透過網路提供服務、授權用户下載、列印、瀏覽等行爲。並得爲符合各資料庫之需求，酌作格式之修改。若爲摘譯、譯稿或改寫稿，需附原作者之正本同意書，並附原文影本一份；來稿如涉及版權，概由作者自負文責。

童綜合醫學雜誌

編著的話

綜　論

原　著

病例報告

臨床病理討論

影像判讀

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